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ARCHIVES OF OPHTHALMOLOGY

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PENETRATION OF PENICILLIN INTO THE EYE

LUDWIG VON SALLMANN, M.D.

AND

KARL MEYER, M.D., PH.D.

WITH THE TECHNICAL ASSISTANCE OF MISS JEANETTE DI GRANDI

NEW YORK

The good results of penicillin in treatment of some experimental intraocular infections of the anterior segment of the eye [1] and the antibacterial activity of penicillin in vitro against most organisms found in intraocular infections suggested the study of the penetration of penicillin into the anterior chamber.

The investigations on the topical use of penicillin deal, first, with the entrance of penicillin into the aqueous of rabbits after iontophoresis as compared with that after the corneal bath; second, with the influence of wetting agents on the penetration of penicillin, and, finally, with the possibility of its introduction by repeated use of solutions or ointments with and without wetting agents. The studies on the systemic application are limited to determinations of penicillin in the blood, the spinal fluid and the intraocular fluids after single intramuscular injections.

The penicillin used in these experiments was obtained from a strain of Penicillium notatum grown by Dr. Gladys Hobby. It was extracted as a relatively crude preparation and converted to its sodium salt in the laboratory of Dr. Karl Meyer.[2] Its inhibitory activity ranged at about 1.24 micrograms per cubic centimeter against a 10^{-1} dilution of an eighteen hour broth culture of Diplococcus pneumoniae type III. Although actual titrations by the Oxford method were not made, 1 mg. of the crude preparation was estimated to be equal to 100 to 150 Oxford units.

TECHNIC

The procedures of iontophoresis and the corneal bath were the same as those described in a previous paper [3] except for the applicator tube, which was constricted near its base for the conservation of fluid. In view of the technic best suited for clinical therapy, local anesthesia was preferred to general anesthesia for iontophoresis and the corneal bath. In the latter procedure a 0.25 per cent solution of sodium penicillin was applied for five minutes; in the former solutions of 0.1 and 0.25 per cent were employed at 2 milliamperes for five minutes.

Three wetting agents were studied. They were aerosol 1B (dibutyl sodium sulfosuccinate), aerosol OT [4] (dioctyl sodium sulfosuccinate) and penetrasol B,[5] which consists of aerosol 1B,

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From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology, Presbyterian Hospital.

1. von Sallmann, L.: Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with Pneumococcus, Arch. Ophth. **30**:426 (Oct.) 1943.
2. Meyer, K.; Chaffee, E.; Hobby, G. L.; Dawson, M. H.; Schwenk, E., and Fleischer, G.: On Penicillin, Science **96**:20, 1942.
3. von Sallmann, L.: Sulfadiazine Iontophoresis in Pyocyaneus Infection of Rabbit Cornea, Am. J. Ophth. **25**:1292, 1942.
4. This drug is supplied by the American Cyanamid and Chemical Corporation.
5. Hermann, F.; Sulzberger, M., and Baer, R.: New Penetrating Vehicles and Solvents, Science **96**:451, 1942.

xylene, propylene glycol and antipyrine. A 0.25 per cent solution of sodium penicillin containing aerosol 1B and penetrasol B, each in a concentration of 1 per cent, was applied in the form of a single corneal bath for five minutes. Control experiments consisted of corneal baths with these wetting agents alone. Zephiran chloride, in a dilution of 1:3,000, as used by O'Brien and Swan,[6] had to be discontinued because its antibacterial activity interfered with the determination of the amount of penicillin. Aerosol 1B and penetrasol B, on the other hand, did not exert any bacteriostatic effect in vitro, nor did they diminish noticeably the action of penicillin.

The solutions for repeated instillation contained 0.25 per cent sodium penicillin alone or with the addition of 0.5 per cent aerosol 1B. The same concentration of aerosol 1B was used for the control experiment. Two drops of each solution was instilled at twenty minute intervals over a period of three hours. Twenty minutes after the final instillation aqueous was withdrawn under sterile conditions.

The ointments, prepared by Dr. Karl Meyer, represented two types of emulsion systems. In the first the free acid of penicillin was dissolved in chloroform and mixed with anhydrous wool fat containing 10 per cent liquid petrolatum. The chloroform was then evaporated in vacuo. The same procedure was followed with the addition of a wetting agent, aerosol OT, in a concentration of 1 per cent. The second type of ointment was an oil-in-water emulsion, from which, according to the experiments of Klein and Scheffer[7] and Klein,[8] the resorption of iodides and alkaloids exceeded about twenty times that from the usual water-in-oil emulsions. The penicillin was dissolved in equal parts of propylene glycol and water to a concentration of 20 per cent of the base, lard U. S. P. Aerosol 1B was added to a sample in a concentration of 0.25 per cent. In all cases except the control experiments with a simple aerosol B salve the ointment contained 0.25 per cent penicillin. Syringes were filled with the salve, and 0.1 cc. was applied to each eye at intervals of thirty minutes over a period of three hours. Thirty minutes after the final application the eyes were rinsed well with nupercaine and aqueous was withdrawn under sterile conditions.

In the experiments on systemic introduction a saline solution containing 20 mg. of sodium penicillin per kilogram of body weight was injected into the hip muscle of the rabbits. Blood was withdrawn at intervals of fifteen, thirty, forty-five, sixty and seventy-five minutes after injection; primary aqueous, at intervals of fifteen, thirty and forty-five minutes; secondary aqueous, at intervals of forty-five and sixty minutes, and vitreous and spinal fluid, at intervals of forty-five, sixty and seventy-five minutes.

The quantitative estimation of penicillin in the ocular fluids, in the blood serum and in the spinal fluid was based on their antibacterial activity. Of the four methods described,[9] the dilution method of Fleming appeared best suited for the purpose of these experiments.

After the given intervals the eyes of the rabbits were anesthetized locally with a sterile solution of 0.1 per cent nupercaine hydrochloride. The surface of the cornea at the place of insertion of the needle was touched with a 3 per cent solution of tincture of iodine, and 0.2 cc. of aqueous was withdrawn from each eye and added to two small culture tubes which contained the same amount of neopeptone broth. Blood, vitreous and spinal fluid were obtained with the usual sterile technic, and two series were set up for each sample. Serial dilutions were made, and to each dilution of the parallel series was added 0.2 cc. of an eighteen hour broth culture of D. pneumoniae type III, diluted 10^{-1} in neopeptone broth. For each group of experiments performed on the same day two control series were run with appropriate dilutions of the same solution of sodium penicillin as that used in the rabbits. The cultures were incubated for eighteen to twenty-four hours and examined for inhibition of bacterial growth. From the bacteriostatic activity of the dilution of penicillin in the control series and the inhibitory action of the tested fluids, the concentration of penicillin in the

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6. O'Brien, C. S., and Swan, K. C.: Carbaminoylcholine Chloride in the Treatment of Glaucoma Simplex, Arch. Ophth. **27**:253 (Feb.) 1942.

7. Klein, N., and Scheffer, L.: Experimentelle Untersuchungen am Auge über die Resorption aus Salben, Arch. f. Ophth. **128**:460, 1932.

8. Klein, M.: Beitrag zur Resorption aus Augensalben: II. Die Resorption des Atropins, Arch. f. Ophth. **129**:413, 1932; Zur Kenntnis der Resorption aus Augensalben: III. Die Resorption des Homatropins, Pilocarpins, und Eserins, ibid. **131**:25, 1933.

9. Fleming, A.: On the Antibacterial Action of Cultures of a Penicillium, with Special Reference to Their Use in the Isolation of B. Influenzae, Brit. J. Exper. Path **10**:226, 1929. Abraham, E. P.; Chain, E.; Fletcher, C. M.; Gardner, A. D.; Heatley, N. G.; Jennings, M. A., and Florey, H. W.: Further Observations on Penicillin, Lancet **2**:177, 1941. Fleming, A.: In Vitro Tests of Penicillin Potency, ibid. **1**:732, 1942. Rammelkamp, C. H.: A Method for Determining the Concentration of Penicillin in Body Fluids and Exudates, Proc. Soc. Exper. Biol. & Med. **51**:95, 1942.

latter was calculated in micrograms per cubic centimeter.[10] Repeated controls with plain aqueous humor were made to exclude any antibacterial effect of this fluid.

RESULTS

Local Applications.—The iontophoretic introduction of a 0.25 per cent solution of sodium penicillin into the aqueous led in forty-five minutes to a maximal concentration of 40 micrograms per cubic centimeter (fig. 1). The average for this maximal concentration was about three times as great as that obtained with a solution of 0.1 per cent sodium penicillin and was almost ten times as great as the average concentration in the aqueous forty-five minutes after a single corneal bath with a 0.25 per cent solution. A small amount of penicillin was found in the aqueous after four hours only with the iontophoretic introduction of a 0.25 per cent solution. The increased speed of penetration under the influence of an electric current is demonstrated by the results of determination of penicillin in the aqueous fifteen minutes after application. Whereas no trace of penicillin was detected after a corneal bath, the presence of 16.6 micrograms per cubic centimeter was

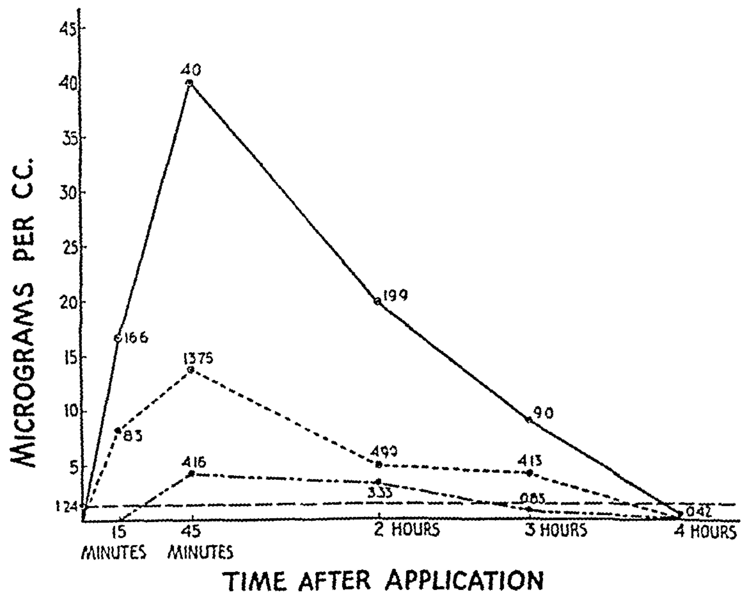

Fig. 1.—Concentration of penicillin in the aqueous humor after application to the cornea. Each figure represents the average of five experiments.

The solid line represents values for iontophoresis with 0.25 per cent solution of sodium penicillin; the line of dots, values for iontophoresis with a 0.1 per cent solution of sodium penicillin; the line of dots and dashes, values for the corneal bath with 0.25 per cent solution of sodium penicillin, and the line of dashes, micrograms of sodium penicillin per cubic centimeter necessary to inhibit growth of D. pneumoniae type III $10.^{-1}$ (The last figure is applicable only to the preparation of the penicillin salt used in the experiments concerned with local introduction.)

estimated after ionization with a 0.25 per cent solution. No detectable amount of penicillin was found in the vitreous which was withdrawn in 2 experiments one hour after the transcorneal iontophoretic introduction of a 0.25 per cent solution of sodium penicillin.

In the first group of experiments with wetting agents nupercaine hydrochloride was employed as the local anesthetic. The addition of aerosol 1B in a concentration of 1 per cent to a 0.25 per cent solution of sodium penicillin applied in the

10. These values are subject to errors inherent in dilution methods. The calculated values for concentration of penicillin in the aqueous do not represent the actual weight of pure penicillin but are relative to the preparations used. It would probably be more accurate to express the concentrations in terms of activity.

form of a corneal bath for five minutes produced in the aqueous an antibacterial activity of 5 micrograms per cubic centimeter, or only slightly more than that obtained with a corneal bath without a wetting agent (fig. 2).

In order that the effect of nupercaine on the permeability of the cornea might be eliminated, general anesthesia with pentobarbital sodium was used in the second group of experiments. The influence of the wetting agent on the penetration of the penicillin solution employed in a corneal bath was more significant under these conditions. The addition of aerosol 1B in a concentration of 1 per cent led to an antibacterial activity of the aqueous which was five times that with a simple corneal bath. The effect of penetrasol B was less pronounced.

Frequent instillations of the 0.25 per cent solution of sodium penicillin with and without the addition of aerosol 1B gave in 2 instances erratic results, but in 4 experiments no inhibitory activity of the aqueous could be detected. In 12 experiments frequent applications of the two types of ointments (page 2) with and without wetting agents did not result in any antibacterial activity of the aqueous. After three hours the irritation of the lids, conjunctiva and cornea, consisting of

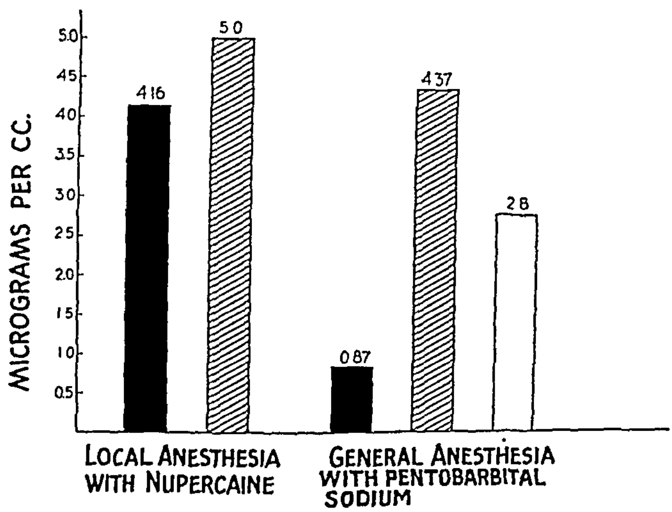

Fig. 2.—Concentration of penicillin in the aqueous humor forty-five minutes after a five minute corneal bath. Each figure represents the average of five experiments.

The black areas represent values for 0.25 per cent sodium penicillin; the cross hatched areas, values for 0.25 per cent sodium penicillin and 1 per cent aerosol 1 B, and the dotted area, values for 0.25 per cent sodium penicillin and 1 per cent penetrasol B.

swelling of the lids, mucopurulent discharge, chemosis of the conjunctiva and haziness of the cornea, was severe with the application of aerosol OT in a concentration of 1 per cent. These signs were moderate or negligible with ointments containing 0.25 per cent aerosol 1B.

The figures on the graph and chart (figs. 1 and 2) represent an average for the results of 5 experiments.

Systemic Introduction.—Of the samples of blood, the first, taken fifteen minutes after the intramuscular injection, showed the greatest antibacterial activity. As figure 3 shows, the amount of penicillin in the blood decreased regularly to about one seventh of its maximum at the end of an hour. The primary aqueous did not inhibit bacterial growth fifteen minutes after injection but demonstrated a moderate antibacterial activity in the samples taken at the thirty and the forty-five minute period. Secondary aqueous, withdrawn forty-five and sixty minutes after injection and thirty minutes after the first paracentesis, inhibited bacterial growth

in considerably higher dilutions than did the primary aqueous. No activity was detected in samples of vitreous and spinal fluid taken at intervals of forty-five, sixty and seventy-five minutes after the injection of penicillin. The figures on the graph (fig. 3) represent an average of the results of 3 to 6 experiments.

COMMENT

Two concentrations of sodium penicillin, 0.1 and 0.25 per cent, were selected for iontophoretic introduction on the basis of previous experiments on intraocular infections and in view of the clinical applicability. With a single application no damage was caused except for transient haziness of the corneal epithelium. With a 0.25 per cent solution the antibacterial activity of the aqueous was evident for almost four hours. The highest concentration, obtained after forty-five minutes, was thirty-two times the amount necessary for in vitro inhibition of a pneumococcus culture in a dilution of $10.^{-1}$ Without use of the electric current the same solution

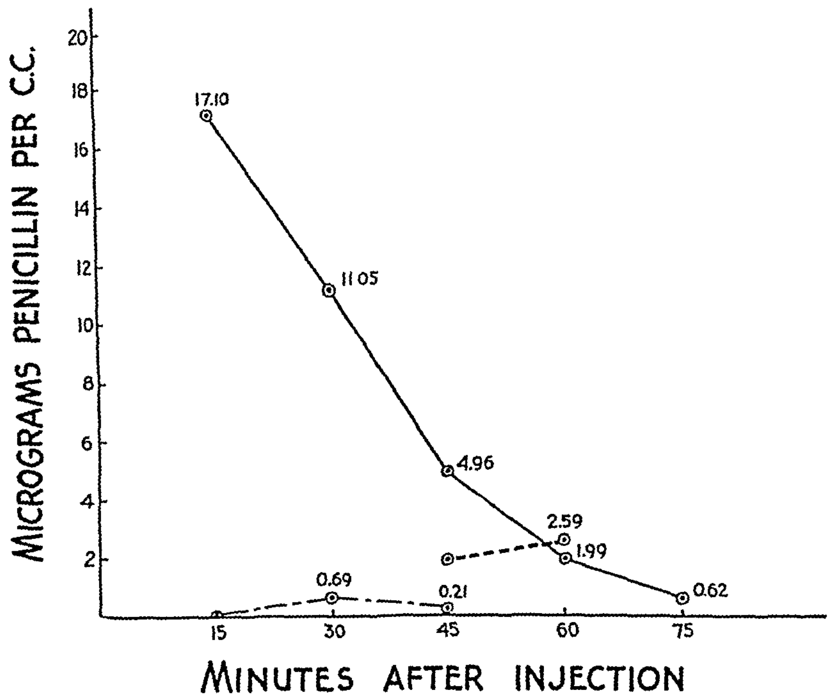

Fig. 3.—Concentration of penicillin in the blood and in the primary and the secondary aqueous of rabbits after a single intramuscular injection of 20 mg. of sodium penicillin per kilogram of body weight. A concentration of 0.415 microgram per cubic centimeter of the sodium penicillin preparation used in this group of experiments was necessary to inhibit growth of D. pneumoniae type III $10.^{-1}$

The solid line represents values for the blood; the line of short and long dashes, values for primary aqueous, and the line of short dashes, values for secondary aqueous.

applied in a corneal bath led to a maximal concentration that was more than three times the amount necessary for inhibition in vitro. Two hours after the corneal bath the aqueous still exhibited an antibacterial activity. These observations explain to a certain extent the surprisingly good results of the corneal bath in the penicillin treatment of experimental pneumococcic infections of the anterior segment of the eye.[1] The therapeutic effect of the corneal bath on such infections was only slightly inferior to that of iontophoresis. As compared with the rapid resorption of penicillin from the blood stream,[11] the rate of depletion from the anterior chamber is moderately slow and is similar to that of sulfadiazine.[3]

11. Rammelkamp, C., and Keefer, C.: The Absorption, Excretion, and Distribution of Penicillin, J. Clin. Investigation 22:425, 1943.

O'Brien and Swan [6] stated that the penetration of carbaminoylcholine chloride into the aqueous can be greatly increased by dissolving it in a vehicle containing a wetting agent, zephiran chloride. Boyd [12] confirmed this activity of zephiran in experiments with physostigmine. According to Gifford,[13] Bellows achieved experimentally an extreme increase in the penetration of sulfonamide compounds into the aqueous by the addition of various wetting agents. In this study with penicillin the addition of aerosol 1B or of penetrasol B enhanced the introduction of the drug in a single application. Penetrasol B was more irritating and less effective. The maximal concentration of penicillin in the aqueous was, however, about one-eighth that achieved with iontophoresis. Furthermore, a comparison of the two groups of experiments demonstrates that the use of nupercaine as a local anesthetic is almost as effective in increasing the penetration of penicillin into the anterior chamber as is the addition of wetting agents to the penicillin solution in its application with general anesthesia. As these experiments were confined to the use of two surface tension depressants, no generalization can be made as to the value of other wetting agents for use with penicillin.

Penicillin applied in salves did not produce any bacteriostatic activity of the aqueous. Conclusions cannot be drawn, however, as to whether the vehicle inactivated the labile compound or whether no resorption occurred from the vehicle. After repeated instillation of the watery solution usually the presence of penicillin was not detected despite the combination with a wetting agent, but two questionable figures indicate that this type of application may give erratic results. Experiments with ointments and instillations failed in their main purpose of providing a means of retention over a longer period of a moderate concentration of penicillin in the aqueous after the steep, but transient, rise following iontophoresis.

The studies were not extended to the estimation of the amount of penicillin in the cornea and lens because the usual extraction methods could not be applied to the labile penicillin without a further increase in the margin of error. Negative results were obtained in 2 experiments with vitreous fluids, withdrawn after the iontophoretic introduction of penicillin.

Rammelkamp and Keefer [11] reported that the spinal fluid of human subjects given intravenous, subcutaneous and intramuscular injections of penicillin did not exhibit any antibacterial activity. The same results were obtained in the experiments reported here with the intramuscular injection in rabbits. The aqueous, however, demonstrated a moderate but definite inhibitory action thirty to forty-five minutes after the injection. The secondary aqueous contained considerably more penicillin than the primary aqueous.

It can be concluded that systemic treatment with penicillin will be beneficial for ocular infections. It is possible that the efficacy of local penicillin therapy, as shown by previous experiments, can be further increased by the combination of topical application and systemic introduction.

SUMMARY

1. The antibacterial activity of the aqueous in vitro served as the basis for determination of the amount of penicillin in the anterior chamber of rabbits after various methods of local application of the sodium salt.

12. Boyd, J. L.: Quantitative Comparison of Methods of Administering Physostigmine. Arch. Ophth. **30**:521 (Oct.) 1943.

13. Gifford, S.: Personal communication to the author.

2. Comparison of the penetration of penicillin into the aqueous after the iontophoretic introduction with that following the corneal bath with and without wetting agents showed that the ionization method increases the concentration of penicillin in the aqueous ten times as much as the corneal bath and about eight times as much as the corneal bath with the addition of a wetting agent, aerosol 1B.

3. After a single iontophoretic application of a solution of the sodium salt of penicillin, the aqueous exhibited an antibacterial activity for almost four hours; after a single corneal bath with a solution of the same concentration, the antibacterial activity continued little more than two hours.

4. Repeated applications of solutions and ointments containing penicillin did not produce any detectable antibacterial activity of the aqueous. The addition of wetting agents was without effect.

5. Small amounts of penicillin entered the aqueous from the blood stream. Secondary aqueous contained several times as much penicillin as primary aqueous.

Columbia University College of Physicians and Surgeons.

PATHOLOGIC CHANGES IN THE LENS ASSOCIATED WITH NONTRAUMATIC IRITIS

BERNARD SAMUELS, M.D.
NEW YORK

In a previous paper [1] I described structural changes in a lens during the active stage of a corneal ulcer as they are seen microscopically, and in a second paper,[2] the changes that may result long after an ulcer has been replaced by scar tissue. The present paper, the third in the series, has for its object a microscopic study of lesions occurring in a lens in nontraumatic iritis.

Ordinarily, a lens remains clear after a first attack of iritis; it is only after repeated attacks that opacities in the lens appear. I recall but 1 case, that of an able-bodied man of 54, in which cataract developed during a first attack of iritis. The iritis lasted about two months and was marked by an enormous infiltration in the stroma and a lenticular mass of exudate in the anterior chamber. The pain was of a rheumatic, intractable character. For a short period the tension was elevated, paracentesis being required to relieve it. After several weeks a sector-shaped area of necrosis appeared in the iris. At the end of the attack opacities appeared in a sector-shaped area of the cortex of the lens. Vision, which had been normal, was reduced to 20/40 and remained so.

Clinically, this case was interesting not alone because of the development of a cataract during a single attack of iritis but because the cataract did not lie under the necrotic sector of the iris. The eye was observed for years after the iritis had subsided. The tension was always normal, and the cataract was stationary.

PATHOLOGIC MATERIAL

In this study, microscopic examination was made of the lenses in 20 globes with nontraumatic iritis. A majority of the globes had been enucleated because of tuberculosis of the uvea, usually of the conglomerate type. In 2 globes Cysticercus was discovered; 1 had been involved in sympathetic ophthalmia, and in 1 a retinoblastoma was present; in 1 globe the condition was mistakenly diagnosed as retinoblastoma, and 2 specimens showed syphilitic iritis.

GENERAL CONSIDERATIONS

Pathologically the symptoms of iritis are commonly classified under two main heads, namely, hyperemia and exudation into the stroma of the iris and into the chambers of the eye. In many physical ways, usually obvious in life, an exudate into the chambers may involve the lens. In mild iritis the pupillary border may become adherent to the capsule of the lens without a demonstrable membrane. In severe iritis, with exudation into the posterior chamber, the entire posterior surface of the iris may be plastered to the capsule of the lens and to the ciliary processes. The pupillary area of the lens may be covered by an exudate—occlusion of the pupil—which may occur independently of an adhesion of the pupil to the lens—seclusion of the pupil. It is known anatomically that every instance of

Read before the American Ophthalmological Society, Hot Springs, Va., June 12, 1943.

1. Samuels, B.: Tr. Am. Ophth. Soc. **39**:66, 1941.
2. Samuels, B.: Tr. Am. Ophth. Soc. **40**:292, 1942.

severe iritis is to some extent accompanied by cyclitis. Hence the word iritis has come to connote iridocyclitis. Owing to the cyclitis, the posterior capsule of the lens may be covered by exudate, which reaches it by way of the vitreous. It is possible for the entire lens to be engulfed in an exudate or to be held in a cyclitic membrane.

In cases of iridocyclitis the position of the lens may be changed so that its capsule and the zonular fibers are put on the stretch, as when an aqueous which is too albuminous or too cellular blocks the spaces of the pectinate ligament and accumulates in the chamber. In this way the depth of the chamber may be increased and the lens pressed backward and compressed against the vitreous. The reverse may happen when a contracting cyclitic membrane throws the lens forward, compressing it against the cornea and the iris. It is known that traction and pressure on the lens, especially when the latter is directed against the resistant cornea, dispose to the formation of the cataract.

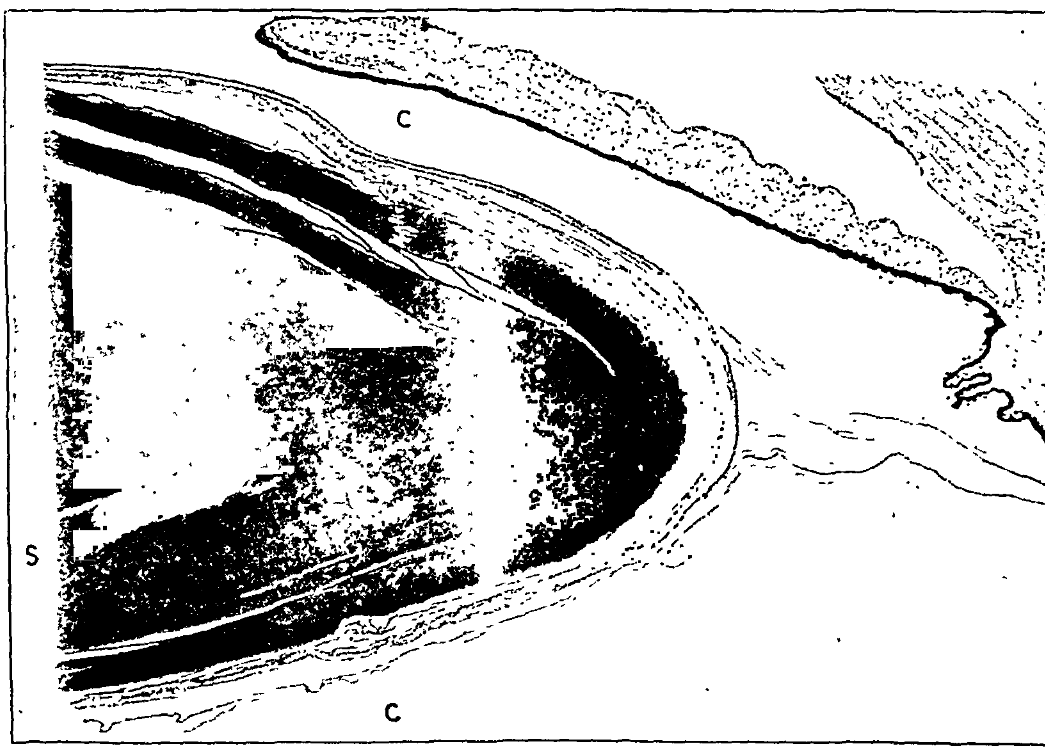

Fig. 1.—Heterochromia, iritis and cataract. The iris is poor in pigment. The angle of filtration is open. The subcapsular layers of the lens are differentiated from the nucleus by their lighter stain and irregularity. At the lower *C* there is a spot of broken-down cortical layer. Similar spots of decay are seen at *S* and the upper *C*. The germinal zone is reduced to a small area, which is considered to be a sign of cataract.

STUDY OF THE MATERIAL

Lesions in the lens, because of the absence of blood vessels in the organ, are regularly referred to as degenerative. The subject is often dismissed with little beyond this statement. Nevertheless, owing to the visibility of the lens in life and its surgical importance, the most minute change within its substance assumes peculiar interest and importance.

REPORT OF SPECIAL CASES

CASE 1.—*Heterochromic cataract* (from a cadaver).

The history stated that the lens had a peculiar bluish gray marking, which had changed little over a long period. In the specimen (fig. 1) there was a narrow stratum of irregular and partially destroyed cortical fibers which extended around the entire circumference of the

lens. In life this zone could not have been quite clear, but was probably translucent—hence the peculiar color. Another remarkable feature was the almost perfect preservation of the subcapsular epithelium in the presence of adjacent diseased lens fibers, a condition indicating that the metabolism of the lens was never much disturbed and accounting for the stationary character of the cataract.

Cases 2 and 3.—*Intraocular cysticercosis.*

The 2 globes containing a cysticercus presented signs of greater toxicity than the eyes with tuberculosis. In 1 case a cysticercus was present in the anterior chamber of the eye. Suddenly, fourteen days before enucleation, a large staphyloma intercalare developed, under which the parasite was visible microscopically. Adjacent to the staphyloma an unusual event had taken place, namely, spontaneous rupture of the capsule of the lens.

In the other case a cysticercus in the vitreous had set up a violent iridocyclitis, causing formation of membranes in the vitreous and detachment of the retina. The interesting features were the disappearance of the posterior capsule of the lens, the invasion of the lens by pus cells and the absence of the entire epithelial system of the lens, resulting in a rare lesion—a "dead lens."

Case 4.—*Sympathetic ophthalmia.*

For eighteen months before enucleation iritis had been present. Because of increased tension, an iridectomy was performed. Shortly after the operation a violent inflammation broke out in the fellow eye, which soon became blind. It could not be proved that this case was one of true sympathetic ophthalmia because spontaneous iritis and secondary glaucoma had ante-

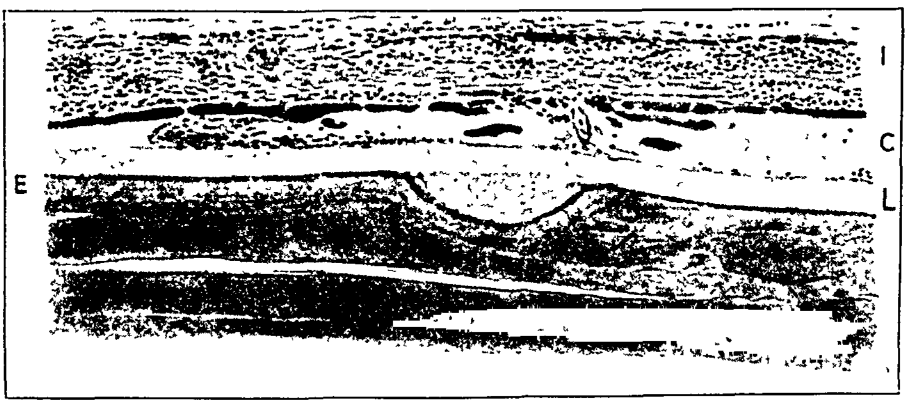

Fig. 2.—An eye removed because of tuberculosis of the retina and secondary glaucoma. The lens is cataractous. A thick layer of hyalinized connective tissue (*C*) binds the iris (*I*) to the capsule of the lens (*L*). The latter is lined by a single layer of epithelial cells (*E*), which at one spot detaches itself from the capsule and dips down into the lens. The space so formed is filled with a homogeneous substance, supposed to be a druse of the capsule.

dated the operation. It may have been a case of bilateral malignant endogenous iritis leading to blindness under the guise of a clinical diagnosis of sympathetic ophthalmia. In such a case the anatomic changes characteristic of sympathetic ophthalmia are present.

Microscopically (fig. 5) the iris was transformed into a tumor-shaped mass, which clinically could have been mistaken for iris bombée. A very cellular subcapsular cataract not only covered the pupillary area but extended beyond the equator on both sides. It demonstrated that a widespread capsular cataract may form in a period of eighteen months.

Case 5.—*Retinoblastoma.*

In this case the pathologic picture did not correspond to the clinical description. The lens had been recorded as opaque, with a chalky white appearance. The lesion proved to be a dense subcapsular cataract, 4 mm. in diameter (fig. 4). If one had undertaken the removal of the lens, one would have been prepared to encounter a hard structure, and not a soft one, lying under a subcapsular cataract. The tumor of the retina lay in contact with the lens The question arose whether the tumor or the iritis had produced the cataract. It was decided that poisonous substances from the tumor first produced the iritis, as sometimes happens in cases of retinoblastoma, and that this, in turn, produced the cataract, after occlusion and seclusion of the pupil.

CASE 6.—*Condition mistakenly diagnosed as retinoblastoma.*

The eye of a boy 6 years of age became blind from secondary glaucoma four weeks before it was enucleated. This case belonged to a small group of cases of iridocyclitis in which, in spite of shrinking membranes and detachment of the retina, glaucoma supervenes and the eye stays hard. It is the fate of most eyes with this condition to be enucleated under a mistaken diagnosis of retinoblastoma. The lens was described as clear. Microscopically (fig. 6), a focus of spindle-shaped cells lay on the internal surface of the capsule posteriorly, in the part of the capsule that bounds the recessus hyaloideocapsularis. In the recessus itself, exactly opposite the focus mentioned, there lay another focus, this one being composed of lymphocytes, epithelioid cells and giant cells. The observations pointed to the following conclusions:

1. A focus of exudation on the external surface of the lens may irritate the overlying epithelial cells so that they produce a focus of cells similar to connective tissue cells.

2. It is possible for the epithelial cells that have proliferated as far back as the ligamentum hyaloideocapsularis to produce spindle-shaped cells, a feat commonly ascribed to the anterior subcapsular cells.

3. The anterior subcapsular and the equatorial cells probably have more in common than is indicated by Salzmann's theory of their being biologically widely different. It is certain that in this instance the posterior, abnormally placed, cells, under the stimulus of an exudate

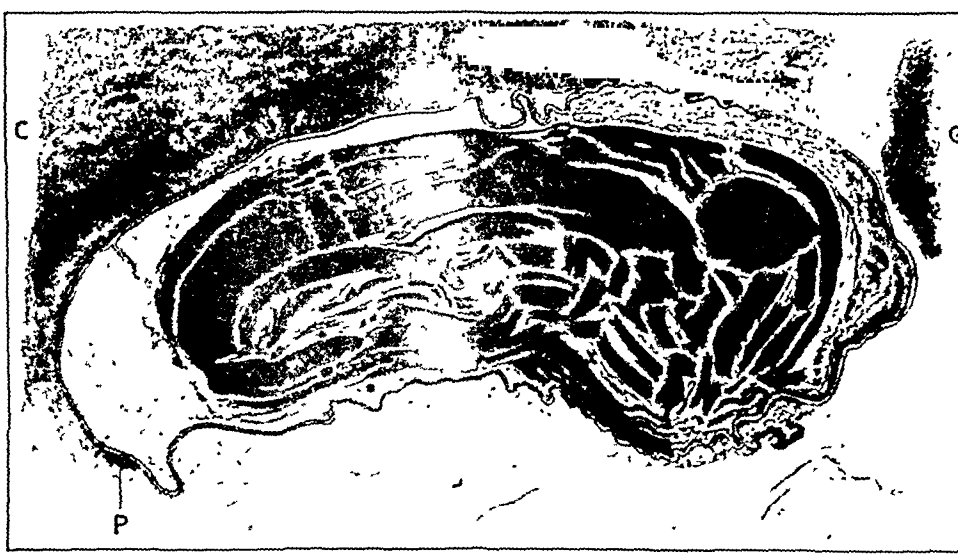

Fig. 3.—In a girl 10 years of age, the entire iris and ciliary body have been replaced by the granulation tissue of tuberculosis (*G*). The lens is shrunken. An eccentric subcapsular cataract extends from the middle of the anterior surface to beyond the equator. The cortical layers throughout and much of the nucleus are liquefied. To the left the capsule is covered with pus cells (*P*), and there the epithelium of the lens is entirely missing.

on the surface, behaved much as the anterior, normally placed, cells would have been expected to do under a similar irritation.

4. Possibly the reason that the anterior subcapsular cells commonly produce a connective tissue-like substance (the subcapsular cataract) and that the equatorial cells seldom do lies not so much in the biologic difference between the two groups of cells as in a dissimilarity of the exciting agents. A noxious substance from an inflamed ciliary body that acts on the equatorial region of the lens is not considered as destructive as one from the cornea that acts on the pupillary region. It is interesting to note that from inflammatory lesions in the body a substance called leukotaxine, responsible for the local migration of leukocytes, as in hypopyon keratitis, has been isolated in pure crystalline form.

CASE 7.—*Druse of the capsule of the lens* (fig. 2).

An abrupt thickening of the capsule was considered to be a druse laid down by the epithelial cells as an expression of malnutrition resulting from an overlying hyalinized membrane. This specimen was reminiscent of the eye with heterochromic cataract in that, while there had been extensive destruction of the cortical layers, the epithelial system showed little alteration in general.

CASE 8.—*Detachment of the germinal zone of the lens.*

A man aged 60 had had a syphilitic infection five months before. Two months later violent iritis broke out, with the formation of a cataract and a pupillary membrane, followed shortly by blindness. Microscopically (fig. 7) there was an unusual combination of an anterior capsular cataract and detachment of the germinal zone of the lens, the latter being due to extensive liquefaction of the cortex. The retina showed enormous infiltration of the internal layers and great thickening of the walls of the precapillaries. As such a rapid and widespread destruction of the lens is not seen in cases of the most severe iritis, probably an error was not made in ascribing the liquefaction to retinitis rather than to iritis.

SUMMARY OF GENERAL PATHOLOGIC CHANGES

Glaucoma.—In 6 cases the existence of glaucoma was mentioned in the history, but in a number of other cases there must have been periods of increased tension, especially in several in which iris bombée was present. Increased tension of itself leads to cataract.

Degree of Iritis.—In every instance, with the exception of the case of heterochromic cataract, extensive adhesions gave evidence that the iritis had been severe.

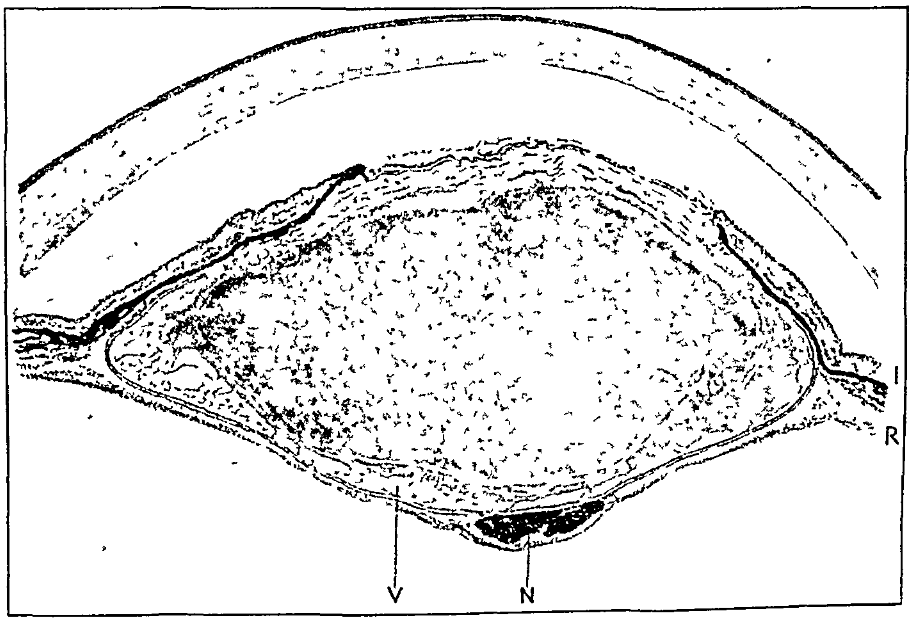

Fig. 4.—A retinoblastoma had led to severe iritis. The retina (*R*) is pressed against the lens, and a nodule of the tumor is shown at *N*. The iris (*I*) is adherent to the lens, the pupillary area of which is covered by a membrane. There is an extensive subcapsular cataract. The concentric particles around the nucleus are fine granules of chalk in the early stage of calcification. The equatorial and posterior capsules are lined by a single row of epithelium, and this, in turn, is covered with vesicular cells (*V*).

Generally, at the posterior pole there was little in the vitreous in the way of exudate or membranes that could have affected the lens physically.

Rupture and Destruction of the Capsule of the Lens.—Rupture of the capsule of the lens in 1 of the cases of cysticercosis and its partial destruction in the other have been mentioned. There was a second case of partial destruction of the capsule, in which the iris had been replaced by a conglomeration of tubercles that filled the anterior chamber. The disappearance of the adjacent portion of the lens capsule was an expression of the malignant property of tuberculosis to erode whatever it touches. Since in all 3 cases the iritis had been exceptionally severe, the conclusion was reached that spontaneous destruction or rupture of the capsule of the lens is an event seldom to be feared in cases of ordinary iridocyclitis. The capsule is brittle but tough.

Folds in the Capsule of the Lens.—In 14 cases the capsule showed folds of various sizes. Ruffling and folds of the capsule are typical of cataract.

Changes in the Epithelium.—In this series of cases of spontaneous iritis the epithelium behaved in ways similar to those observed in the cases of corneal scar. There were 8 cases of extensive subcapsular cataract, in several of which it straddled the equator.

Death of the Subcapsular Epithelium.—In the entire series there was only 1 instance, a case of cysticercosis, in which the entire epithelium had disappeared so that the lens was really "dead." In view of the great amount of destruction of the substance of the lens in some of the cases, it is remarkable that the epithelium should have been spared.

Changes in the Substance of the Lens.—In general, the changes in the substance of the lens in this series differed little from those in the 36 lenses described in the paper on corneal scar.[2] As a special feature in this series, subcapsular vacuoles were present in most of the lenses. In 1 lens the vacuoles were confined to the posterior cortical layers and were in contact with the capsule. In this lens the substance should have shelled out easily in an extracapsular extraction. Some

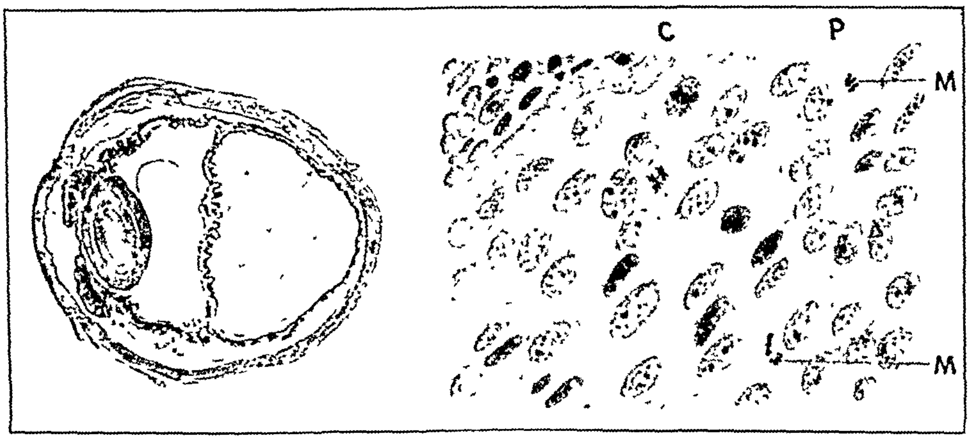

Fig. 5.—Sections in a case of sympathetic ophthalmia. At the left is shown the tumor-like infiltration of the iris, which clinically simulated iris bombée. A nodular infiltration is seen in the ciliary body and in the choroid. In the detail to the right, the capsule of the lens (*C*) is covered with lymphocytes and epithelioid cells from the iris. The mass of cells on the posterior surface of the capsule (*P*) represents rapid proliferation of the capsular epithelium. A few mitotic figures (*M*) are visible, an unusual observation. The cells of the cataract bear a striking resemblance to those of the infiltration in the iris.

lenses showed extensive liquefaction and calcification of their substance. In 2 lenses the liquefaction went so far as to produce a genuine morgagnian cataract. Occasionally a lens was decidedly swollen.

Vesicular Cells.—Vesicular cells were noted less often in the present series than in cases of corneal scar, although in 4 lenses they were numerous. It is worthy of note that in 2 lenses vesicular cells were located beneath the anterior capsule, at a distance from their usual site at the equator. In 1 lens the germinal zone was replaced by a large group of vesicular cells. In another lens a great cavity was seen in the germinal zone which was probably produced by the bursting of vesicular cells and their confluence.

SPECIAL TYPES OF PROLIFERATION OF THE EPITHELIUM OF THE LENS

Flat Proliferation.—Several times after the disappearance of the germinal whorl, the capsule at the equator was left completely bare of epithelium. More often

a single row of epithelial cells remained in immediate contact with the capsule and proliferated backward until it lined the entire posterior capsule. This is an occurrence especially characteristic of cataract following detachment of the retina. At the posterior pole, as a rarity, vesicular cells were interposed between the row of epithelial cells and the nucleus of the lens. The impression was gained that the presence of one type of cells excludes the presence of the other. It seemed that when the medium was not favorable for the formation of vesicular cells, the cells restricted their proliferating power to growing backward along the surface of the capsule. It was noted that the lenses in which the epithelium had lined the capsule throughout were the lenses that showed the greatest amount of liquefaction of the substance. Conversely, a group of vesicular cells was associated with lenses having better preserved substance.

Massive Proliferation.—This type was represented by the fully developed anterior subcapsular cataract. When the anterior subcapsular cataracts in this series and those in the series of cases of corneal ulcer and corneal scar were considered together, enough diversity was noted to suggest the following subtypes:

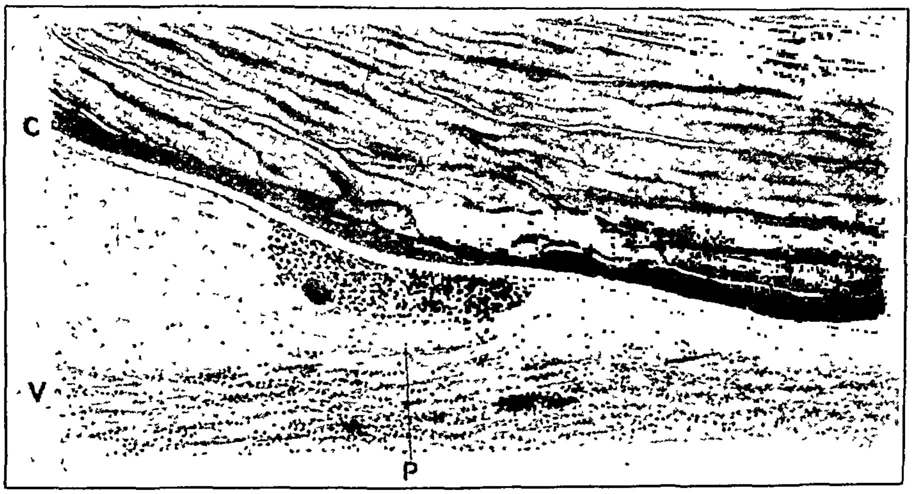

Fig. 6.—The eye of a 6 year old boy who had been blind for four weeks due to the presence of a lesion mistakenly diagnosed as retinoblastoma. In the recessus hyaloideo-capsularis, lying between the capsule of the lens (*C*) and the vitreous (*V*), there is a precipitate (*P*) containing a large giant cell. Overlying this the capsule of the lens shows proliferation of spindle-shaped cells. To the left, toward the equator, the epithelium is normal, but to the right, toward the posterior pole, the epithelium is flat and scanty.

1. Widespread Type (figs. 3 and 4) with an Undulating Anterior Surface: In 1 case a cataract of this type attained a diameter of 6 mm., and in rare instances the lesion straddled the equator. The cataract consisted of spindle-shaped cells which had laid down a homogeneous, tough substance. It was frequently lined on its posterior surface by a layer of epithelium continuous with that lining the capsule.

2. Circumscribed Pyramidal Type, Projecting Abruptly Forward in a Cone: Frequently the cataract was located in the exact center of the pupil. Its substance was cellular. It was not easy to understand why the proliferation in this type was so circumscribed and often entirely isolated from the pupillary border of the iris. The production of a pyramidal cataract is commonly ascribed to irritation from the cornea, such as that due to a serpiginous ulcer. However, a pyramidal cataract is not infrequently encountered in cases of detachment of the retina after

inflammation has set in, proof that it may also be caused by an irritating substance coming from the posterior zone of the eye.

3. Type Characterized by Numerous Sharp Wrinkles and Folds of the Anterior Capsule: The stroma consisted of a thin, loose filamentary proliferation of the epithelium.

SIMILARITY OF SUBCAPSULAR CATARACT AND CALLUS *(SCHWIELE)* OF THE CILIARY BODY

The interior of the lens is not the only place in the eye in which the epithelial cells may lay down a substance similar to that of an anterior capsular cataract.

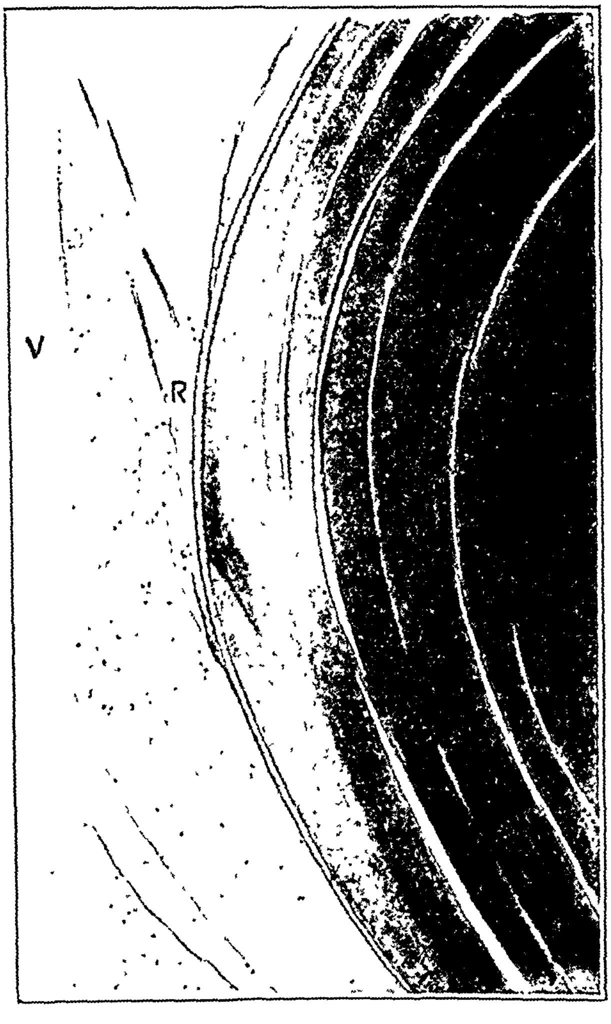

Fig. 7.—Syphilitic iritis in the eye of a man aged 60, who had been blind for three months. A subcapsular cataract (not shown) developed in the pupillary area. At the equator the germinal zone is detached from the capsule. The vitreous (*V*) is pushed forward by the detached retina, and therefore the recessus hyaloideocapsularis (*R*), which as a rule is directed frontally, is here directed anteriorly. The space contains a few red blood cells.

Occasionally, in the study of subcapsular cataracts a similar massive formation lying on the flat part of the ciliary body or on the choroid is encountered. In the latter location the pigmented epithelium may join the nonpigmented epithelium in its formation. A comparison of these connective tissue-like formations of epithelial origin in the various locations never fails to be of interest.

THEORIES OF THE CAUSES OF SUBCAPSULAR CATARACT

In general, the cataracts described in the series of corneal scars were larger than those associated with corneal ulcers. There was no doubt that the smaller

cataracts which developed during the active stage of an ulcer represented the direct response to irritation produced by bacterial action. For the development of the larger cataracts found in the series of cases of corneal scar there must have been some other factor. At the moment of perforation of an ulcer the products of the bacteria are washed out with the aqueous and no longer can accumulate during the fistulating and healing processes. Freedom from bacterial poisons after perforation of an ulcer accounts for the rapidity with which the inflammation in such an eye disappears. I came to the conclusion that faulty metabolism is a factor in the production of the large cataracts seen in eyes with old atheromatous scars of the cornea. The accompanying pigmentary degeneration of the retina in such eyes speaks in favor of a disturbed metabolism throughout the eye.

With respect to the previously mentioned clinical case of a cataract which developed at the end of a single attack of iritis, it was my opinion that the cataract was the result of faulty metabolism in the lens. If the substance leukotaxine from the inflammatory lesion in the iris had been the cause, the cataract should

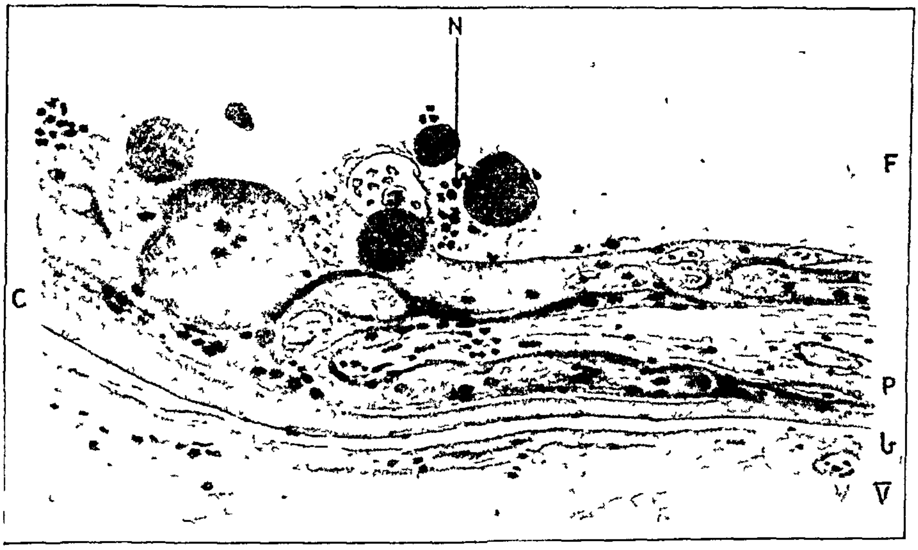

Fig. 8—A complicated cataract in a case of tuberculosis of the iris. Toward the right, at *P*, is a layer of vesicular cells. At *N* is a group of nuclei, which represent cells originating outside the lens. Most of the nucleus (*F*) is fluid The vitreous (*V*) shows some cells and fibroblasts *C* is the capsule of the lens, and *b*, a blood vessel

have developed during the acme of the attack. The faulty metabolism was attributed to damage suffered by the ciliary body during the prolonged attack of iritis. However, the damage could not have been great because the tension of the eye returned to normal and the cataract did not increase.

The fact that the epithelium and the substance of the lens may both be destroyed by a substance derived from an inflammatory lesion is not to be minimized. This occurs rapidly in association with necrosis of a sarcoma of the uvea and metastatic ophthalmitis. However, because of its inert quality, the lens seems to be able to withstand the mild production of leukotaxine in each attack of recurrent iritis and does not become cataractous until the ciliary body is no longer able to nourish it properly. Analogously, in a case of acute fulminating glaucoma that subsides spontaneously, the ciliary body undergoes changes, although unseen clinically, which are similar to the atrophy and necrosis obvious in the iris. Hence it is that after the attack, in spite of the permanent blockage of the angle of the chamber, the eye may become soft and remain so, the ciliary body being unable

to secrete the normal quantity of aqueous. Nevertheless, the lens takes on a characteristic greenish color and in the end, because of malnutrition, becomes cataractous.

PROLIFERATION OF EPITHELIUM AS AN ATTEMPT AT RESTORATION OF THE ORGAN

In many specimens it was noted that the disintegration of the lens fibers seemed to have antedated the proliferation of the epithelial cells. The massive type of proliferation in shape often resembled a biconvex lens. If the substance of the new formation had been of such nature and regularity as to have assured transparency in the living eye, there would have been no doubt that it represented a true lens superimposed on the original nucleus.

An anterior lenticonus in shape also suggests a small lens superimposed on a larger one. It would be interesting to know whether an anterior lenticonus is a symbol of an irregular and luxuriant activity of the subcapsular epithelium during embryonic life.

NUTRITION OF THE LENS

Throughout the entire study it seemed to be more than a mere coincidence that the epithelial system of a lens confines itself normally to that portion of the capsule bathed in aqueous. That the aqueous can nourish epithelial cells is proved by pathologic observations. Epithelial cells extruded from a rent in the capsule may live free in the anterior chamber indefinitely. Likewise, cells of connective tissue origin may live free in the aqueous. As an example, in cases of sarcoma of the ciliary body detached cells, well nourished, may be seen clinging to and creeping along the zonular fibers.

In the present preparations the epithelial cells that lined the capsule at the posterior pole, notwithstanding that they were anatomically identical with those at the anterior pole, never produced a posterior subcapsular cataract in the sense of an anterior subcapsular cataract. One can speculate that the cells in their new position had not within themselves the power to multiply or that the vitreous did not afford them the required nourishment or that there was no incentive to proliferate.

57 West Fifty-Seventh Street.

THE SOCKET AFTER ENUCLEATION AND THE ARTIFICIAL EYE

THEODORE J. DIMITRY, M.D.
Director of Department of Ophthalmology and Professor of Ophthalmology,
Louisiana State University School of Medicine
NEW ORLEANS

HISTORICAL REVIEW

Simple enucleation is not the most ancient surgical means of ridding the orbit of the eye. On the contrary, other surgical procedures were adopted until one hundred years ago. In the earlier period an operation that peeled the eye from its capsule was considered brutal as compared with procedures in which the eye was cut open rapidly and the contents eviscerated. To accomplish the latter, it was not unusual to cut away the cornea.

Recall what was designated in an earlier period (1583) as an extirpation—today justifiably denominated the butchery of George Bartisch.[1] He transfixed the eye, having passed through it a large curved needle threaded with tape, and then, pulling on the tape, cut the eye away.

Though Cleoburey [2] introduced the classic enucleation of the eye in 1826, his procedure was not adopted until 1855. Its performance was naturally slow, requiring dexterity and skill. Anesthetics had not yet been discovered. Ferrall [3] and Bonnet [4] have for years been given credit for having originated the procedure of enucleation. However, it is now admitted that the operation was not instituted by them. Cleoburey [2] described the enucleation operation as follows:

OF THE REMOVAL OF THE GLOBE OF THE EYE

> The conjunctiva should first be divided with a thin sharp-pointed knife, and next all the muscles inserted into the globe: this being done, the point of the knife would be carried cautiously backwards to the posterior part of the orbit, and the optic nerve divided: the nerve will be more easily divided by directing the knife backwards into the orbit on the nasal side of the globe, as the optic foramen is situated nearer on this side from the centre of the orbit. The operator should be careful not to injure the thin orbitar plate of the frontal bone, otherwise the brain may be injured, and in dividing the nerve, he should avoid stretching it. Very little hemorrhage succeeds this operation, unless the vessels are diseased, when it may be restrained by pressure; the dressings should be as simple as possible.[5]

Ferrall introduced the description of his procedure with the following prefatory comment, and I shall fashion my contribution about these truths.

> If it be true, that the clinical studies are most productive which are based upon correct anatomical knowledge, it must also be admitted, that the researches in anatomy are most

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It is in keeping with the spirit of the day that relentless search be made to improve all works of man.

1. Bartisch, G.: Augendienst, Dresden, M. Stöckel, 1583.
2. Cleoburey, W.: A Review of Different Operations Performed on the Eyes, London, T. & G. Underwood, 1826.
3. Ferrall, J. M.: Dublin J. M. Sc. **19**:329, 1841.
4. Bonnet, A.: Ann. d'ocul. **5**:1841.
5. If this statement is true, why should gauze be jammed into the socket after the enucleation; why is the figure-eight bandage tightly applied, and why is hot water used to control "very little hemorrhage"?

profitable to which we are forced to return, by phenomena in disease, unexplained by, or irreconcileable [sic] with the current notions of the structures engaged. It would be an easy and not unpleasing task, to maintain this proposition by a reference to the medical literature of almost every country in civilized Europe.[3]

It must be remembered that it was Jacques René Tenon, French anatomist and oculist, 1724-1816, who discovered the fascia bulbi, from which the eye is peeled, whereupon the cue which set one's wits to work was provided.

However, it is well recognized that even Tenon cannot be given priority for discovery of the fascia bulbi, for Galen, Columbo, Casserinus, Riolon and others had already described this tunic. It was Tenon, however, who described it fully; yet Whitnall[6] stated, in April 1921: "It is the subject of reinvestigation and labored description," and Dwight added: "The complications of this membrane are limited only by the perverted ingenuity of those who describe it."

DEFINITION AND DESCRIPTION

The simple enucleation is here defined as the peeling of the eye from Tenon's capsule. Random severance of muscles and tissues to rid the orbit of the globe is not enucleation but extirpation—however, not the butchery of Bartisch. Though the eyeball is removed entirely by extirpation, enucleation demands that it be shelled out as one does the kernel of a nut. The simple enucleation removes 6.5 volume measurements of the orbit's contents.

When the eye is shelled from the capsule, the muscles are cut from the sclera, but not from the capsule. The belief that the rectus muscles when cut at their attachment to the eye retract extensively is erroneous. Duke-Elder[7] stated:

> The muscles are covered by fascial sheaths continuous with Tenon's capsule. At the point where the two fuse, the connection between the muscle fibres and the sheath is especially strong, so that after enucleation of the globe, the muscles retain their attachment to the capsule, and do not retract extensively.

But if, during enucleation, the muscles are cut through the muscle tissues, not the tendon, and outside the capsule, distal to the fascial sheaths, there is a noticeable retraction of the muscles and tissues backward into the orbit, and if the check ligaments are also cut, increased disfigurement of the socket is produced.

Many surgeons assume that a concave cavity is left in the socket after the globe has been removed. Grimsdale and Brewerton[8] stated:

> The fat and muscles remaining after the removal of the eye fall together in the orbit and form a concave stump, against which the artificial eye is placed.

This is true regarding improper enucleation but erroneous regarding proper enucleation. In addition, the same authors stated:

> The prothesis is concave, and between it and the concave stump a large space is left, in which the secretions accumulate, and, decomposing, irritate the conjunctiva.

The assumed cavity was so definite in the mind of Müller,[9] an artificial eye artisan, that he developed a double shell eye made of glass and on the under belly supplemented a ball to fit the supposed hollow.

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6. Whitnall, S. E.: The Anatomy of the Human Orbit, London, H. Frowde, Hodder & Stoughton, 1921, p. 288.
7. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 1, p. 179.
8. Grimsdale, H. B., and Brewerton, E.: Textbook of Ophthalmic Operations, ed. 2, New York, William Wood & Company, 1920, p. 186.
9. Müller, J.: United States Government patent, 1899.

So, based on certainty that a concavity was left after enucleation, a popular surgical procedure of today provides that a ball be implanted into the capsule of Tenon.[10] The rationale of such a procedure is not clear, for the socket left after such an operation is much the same as that which follows the enucleation. One need but open the lids of patients subjected to enucleation and of those operated on by implantation of a ball into Tenon's capsule to realize that surmises governed instead of facts (fig. 1).

The following declaration is not so readily proved: viz., that after the enucleation of the eye, the tissues come forward in the orbit. Translatory movements of the eye and translatory movement of the socket's tissues after the eye has been peeled out are matters of some importance in clinical ophthalmology and in ophthalmic surgery, for if shown to exist they help to establish the enucleation procedure as having even greater merit than was originally assumed.

Duke-Elder made the following statement (page 581)[7]:

The movements of pure translation (forwards and backwards and from side to side) which are normally permitted to the eyeball are small. If the palpebral aperture is forcibly widened the relief of pressure allows the cornea to move slightly forwards (1 mm., J. Müller [11] 1868;

Fig. 1.—Characteristic photograph of the socket after enucleation. The depth is seen as a plane tilted backward at the outer upper angle; a ball implanted into Tenon's capsule gives the same picture. A semisphere, with the same dimensions as those of the human eye, and held fast to this plane, may move to a remarkable extent.

0.8 mm., Tuyl,[12] 1901) as well as downwards and inwards (Berlin,[13] 1871) and a converse backward displacement accompanies contraction of the lids. These movements are passive and depend on the slight extent to which the orbital fat may be moved and on the pull of the levator palpebrae upon the septum orbitals (Ludwig,[14] 1904; Peschel.[15] 1904; Birch-Hirschfeld,[16] 1912).

It is the pull of the rectus muscles on the globe which compresses the fat of the orbit, and the fatty tissue, although relatively incompressible, is altered in position and shape so that it comes forward in the orbit when unrestrained. It is not simply an engorgement of tissues, which immediately fall into the gap left after enucleation

10. Lang, W.: Tr. Ophth. Soc. U. Kingdom **7**:286, 1887.
11. Müller, J.: Arch. f. Ophth. (pt. 3) **14**:183, 1868.
12. Tuyl, G.: Arch. f. Ophth. **52**:233, 1901.
13. Berlin, T.: Arch. f. Ophth. (pt. 2) **17**:193, 1871.
14. Ludwig, P.: Klin. Monatsbl. f. Augenh. **41**:389, 1904.
15. Peschel, M.: Centralbl. f. prakt. Augenh. **28**:11, 1904.
16. Birch-Hirschfeld, in Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Berlin, Julius Springer, 1912, vol. 9, pt. 2.

or the fat is unleashed, but the action of the oblique muscles, the check ligaments and the elastic qualities inherent in Tenon's capsule which are concerned.

The oblique muscles participate actively in the forward pull of the tissues, particularly noticeable after enucleation, which leaves revealed a ridge in the socket in evidence of the function of the oblique muscles, and for centuries the artificial eye has been designed to avoid this ridge.

Analysis of the pattern of the anterior segment of the eye, made as though one were preparing a mold for the contact lens, and of the pattern of the socket after enucleation reveals that but one-half the eye appears to have been removed at the time of enucleation. After a classic enucleation, the artificial eye used to replace the normal eye is less than 12 mm. in thickness, though ample to set well

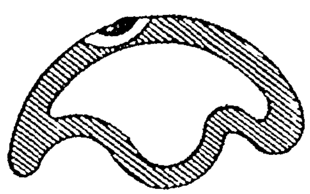

Fig. 2.—In 1899 Müller made the concave surface of the glass eye bulbous. This was done in conformity with the teaching that the enucleated socket was concave.

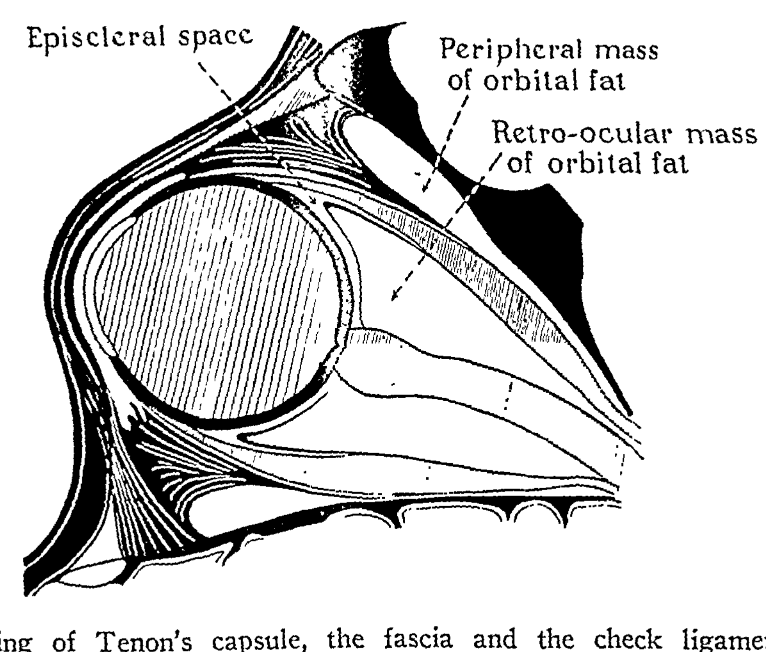

Fig. 3.—Drawing of Tenon's capsule, the fascia and the check ligament, showing how the triangular ligament participates in the formation of the ball and socket joint. The fascia of the muscles is continuous with the check ligament. Though the drawing does not show the oblique muscles, it demonstrates how the superior oblique muscle turns backward at the trochlea, at an angle of 54 degrees. The superior oblique muscle is inserted by fascia into Tenon's capsule and the posterior central portion of the sclera, and the inferior oblique muscle is attached by the fascial sheaths to the posterolateral aspect of the globe.

forward in a position similar to that of the normal eye. The socket, after enucleation, moves forward approximately 12 mm.

If the teachings of René Descartes, the French philosopher, with regard to the physiologic basis for reciprocal innervation, common to opposing muscles, are accepted, then the hypothesis that the oblique and rectus muscles function reciprocally is established.

SEWING OF RECTUS MUSCLES

It is readily demonstrable clinically that improvement, cosmetic or other, does not follow on the sewing of opposing rectus muscles but that, on the contrary, disfigurement of the socket is produced. Closure of the wound in the horizontal plane reduces the upper and the lower cul-de-sac; closure in the vertical plane reduces the lateral cul-de-sac, and the pouch string suture reduces both. Moreover, sewing creates distortion of the fascia, the check ligament and the orbital septum. Most surgeons realize that these things happen. John Green, of St. Louis, repeatedly stated, so I am informed, "that he seldom sewed the wound." His rationale for not doing so may not have been fully explained, but he undoubtedly had a remarkable understanding of the problem. Perhaps he visualized the eyes being wedged into the capsule in ball and socket fashion by the check ligaments and the manner in which these ligaments, the fascia and the capsule were altered by sewing.

The eyelid, in order to open and close, must be supported from beneath as though it were sliding on a fulcrum. Unsupported, the lid's lag is much like a ptosis. It is remarkable to witness how quickly the ptosis is overcome when an artificial eye is inserted into the enucleated socket; the modus operandi is that of the levator palpebrae muscle, which functions and elevates the lid only when its aponeurosis is expanded in archlike form over a fulcrum.

It was the opinion expressed by many authors that the disfigurement of the sulcus following the enucleation could be corrected if a bolster-like cushion was placed atop the prothesis. The crutch of Colomb [17] and that of F. and A. Müller [18] are examples of efforts to accomplish correction of such a fault by physical means. Duke-Elder [7] explained why the physical means made the condition worse instead of better (p. 173).

> The levator palpebrae superioris arises at the apex of the orbit from the lesser wing of the sphenoid above the annulus, its origin blending inferiorly with that of the superior rectus and medially with that of the superior oblique. It runs forwards under the roof of the orbit and upon the superior rectus, the medial borders of the two muscles being adherent by fascial sheaths, and it terminates in an expanded aponeurosis in the upper lid.

Further, it should be recalled that the fascial sheath fuses the levator palpebrae with the superior rectus muscle as they pass to their several insertions. One needs only to pull on the superior rectus muscle after enucleation to produce the characteristic sulcus that follows the operation. One should prevent by any reasonable means the vertical (superior and inferior rectus) muscles from being brought together.

A means of some merit in overcoming the pull on the superior rectus muscle, and indirectly on the levator palpebrae, is to crisscross narrow, undermined bands of conjunctiva between the muscles. Another method is to sew the superior rectus muscle to the levator palpebrae muscle and the tissue about it. However, the best way is to introduce an interim prothesis, such as I have developed. It is made of a transparent plastic with notches at the periphery, one above and one below, to be fitted about the ridge produced by the oblique muscles, and with a large aperture in the center for accomplishing this replacement of tissues and for drainage.

ENUCLEATION VERSUS SUBSTITUTE PROCEDURES

Soon after the simple enucleation had been adopted, its condemnation was heard. As late as 1917 I [19] contributed an article, entitled "Enucleation of the Eyeball A

17. Colomb, P.: United States Government patent 182539, 1905.
18. Müller, F., and Müller, A.: United States Government patent 5183-821, 1912.
19. Dimitry, T. J.: New Orleans M. & S. J. **69**:205, 1916-1917.

Faulty Technic, Cosmetically Considered," and another "Operation Relegating Enucleation of the Eye."[20] Now, with greater knowledge and experience, I advocate what I apparently condemned, my alibi being that the operation I was familiar with at the time of the first writing was an extirpation of the globe, and not an enucleation. Others continue to extirpate, thinking they enucleate the eye.

Mules[21] was the first to register dissatisfaction with the simple enucleation. Instead of getting rid of the globe, he eviscerated the sclera, after having removed the cornea and inserted a glass ball. This was in 1884. In 1920, Grimsdale and Brewerton[8] commented: "This method with slight modification only remains the best cosmetic operation." In time the Mules scleral implant operation met not only with criticism but with condemnation. Nicati,[22] Ray,[23] Hall,[24] Huizinga[25] and I[26] attempted to salvage the Mules procedure. Though these workers removed the source productive of sympathetic ophthalmia, that which condemned it, and made cosmetic improvements in the socket for the artificial eye to rest on, the eye remained immobile. And as the operation was developed to obtain mobility for the prothesis, it lost favor.

I developed a procedure[20] which retained the one-third loss that was required in the Mules operation and did away with the artificial glass eye. I implanted a color ball behind the transparent cornea and demonstrated that the cornea remained transparent, with a pleasing effect, but the cornea thinned to such an extent that it no longer retained the color ball.

The Frost operation[27] should be classed not as a substitute for, but as an adjunct to, simple enucleation. In this operation a 10 to 12 mm. ball is sewn within Tenon's capsule after the globe has been peeled from it. The implanted ball is small, and both the muscles and the capsule are sewn over. Its accomplishment requires that the fascia of the bulb and the muscles, with their attachment to the check ligaments, be drawn on. The operation was performed to restrain the muscles from retracting and in the hope of obtaining a cervix-like stump; however, the muscles normally do not retract, and no such stump is produced.

The body implanted into Tenon's capsule is most commonly spherical. However, there are two exceptions. Berens[28] implants a plastic body in Tenon's capsule which is shaped like a semisphere atop a cone; the apex of the cone sits deep in the cone of the rectus muscles. He wanted to prevent the ball from becoming herniated, as is common when the spherical body is implanted. In the past I have advocated a plastic implant shaped like a semisphere topped by a prism (fig. 4). The prism's ridge, when the plastic body is inserted into Tenon's capsule, faces forward, and the ridge is placed so as to run between the vertical rectus muscles and permits exact sewing of cut edges. The ridge, when the prism atop a semisphere is sewn in the capsule, acts as a horse for the prothesis to rock on, and it has the effect of reducing the disfigurement, such as follows when the superior

20. Dimitry, T. J.: Am. J. Ophth. **2**:653, 1919.
21. Mules, S. H.: Tr. Ophth. Soc. U. Kingdom **5**:200, 1885.
22. Nicati, W.: Arch. d'opht. **232**:347, 1903.
23. Ray, V.: South. M. J. **10**:594, 1917.
24. Hall, E.: Am. J. Surg. **7**:96, 1896.
25. Huizinga, J. G.: Eviscero-Neurotomy: A New Operation, J. A. M. A. **34**:394 (Feb. 17) 1900.
26. Dimitry, T. J.: South. M. J. **10**:594, 1917.
27. Frost, W. A.: Brit. M. J. **1**:1150, 1887.
28. Berens, C.: Am. J. Ophth. **23**:805, 1940.

rectus muscle is pulled on and indirectly pulls on the levator muscle of the upper lid. The first was accomplished, but the artificial eye I had used up to that time would not move.

THE MOBILE PROTHESIS

The ophthalmologist has been diligent in his efforts to obtain a mobile stump; he sought, however, by such means to obtain a mobile prothesis. He has obtained the mobile stump, but he has been unsuccessful in obtaining the mobile prothesis.

Neither the supplemented enucleation procedures nor the substitute operations have advanced the mobile prothesis, and the simple enucleation is found to produce

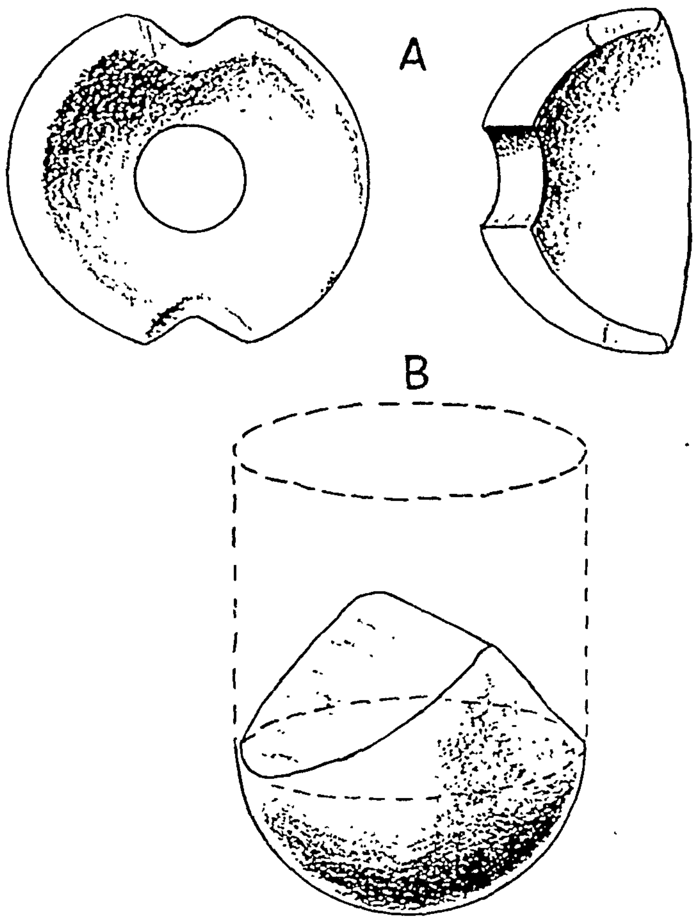

Fig. 4.—*A,* the Dimitry interim prothesis, made of a transparent plastic. It is 23 mm. in diameter and approximately 3 mm. thick. The notches above and below are to hold the muscles apart.

B, the Dimitry semisphere-prism implant is made of a plastic. The parts are of different diameters—10, 11 and 12 mm. When the implant is placed in Tenon's capsule or the sclera, the ridge is pushed forward, and the cut edge of the wound is sutured over it. The ridge runs vertically and holds the vertical rectus muscles parted.

a stump with motion, when calibrated, equal to the motion following the substitute procedures. The problem is not that of tissue mobility but that of the artificial eye.

THE OCULARISTS

The ocularists, artificial eye artisans, had their beginning in ancient days, and America may have led in the ambition to cover a blemish left after the eye was lost. The Incas Indians placed under the lid, to cover a blemish, little stones assembled in mosaic formation.

Paré was the father of surgery, and also the father of the artificial eye (1509-1590). He wrote as follows regarding this:[29]

METHOD OF FITTING AN ARTIFICIAL EYE

I have already treated fully tumors, wounds, ulcers, fractures and dislocations, for which the three functions of surgery are employed, namely: to join what is separated, to remove what is superfluous and to separate what is joined. It remains now to speak briefly of the fourth, which is to supply what is wanting, either through fault of Nature or through accident. . . . One often sees eyes that are deep set, protruding from their sockets or shrunken by reason of a blow or an inflammation. Sometimes when such an accident follows the healing of an ulcer, one can fit an artificial eye, such as the ones shown here, which serves only to improve the appearance of the patient.

Artificial eyes, some of which are shown [in figure 5], are made of enameled gold and are colored like natural eyes.

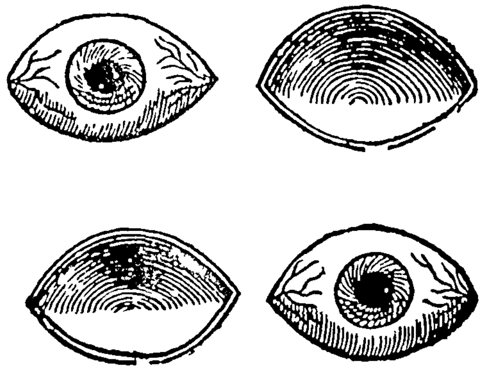

Fig. 5.—Artificial eye of Paré.

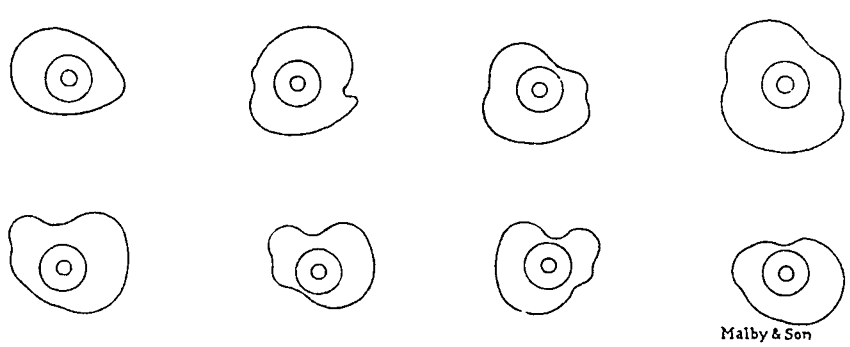

Fig. 6.—Artificial eye of Boissonneau (1854).

Desjardins and Boissonneau,[30] as early as 1866, made Paris the mecca for artificial eyes. Boissonneau was an artisan, not an oculist; Desjardins was an oculist. Boissonneau's[31] artistic ability was communicated to Müller, who, having acquired fully from this source, carried his knowledge back to Germany and capitalized on it.

The original glass eye came from the Greeks of Dalmatia. During the Latin war, after the defeat of the Greeks, the knowledge was taken to Venice and then into Germany. Paré, Desjardins and Snellen were the three with medical knowledge who were interested in the artificial eye.

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29. Paré, A.: Les oeuvres de M. Ambroise Paré, conseiller et premier chirurgien du roy, Paris, G. Buon, 1575, book 23, chap. 1.

30. Footnote deleted by author.

31. It was said of Boissonneau, "He traveled the country looking up one-eyed people to fit with his created prothesis."

Jeyes[32] (1892), of England, produced an artificial eye that was to sit forward in the socket and distend the upper lid so that the objectionable ptosis and disfigured sulcus would be corrected. The eye was of enameled metal; to its under belly was attached a spring within a cylinder, the latter provided with a plate to rest on the socket's tissue.

Fig. 7.—Artificial eye of Jeyes (1892).

Fig. 8.—Artificial eyes of Müller (1907).

In 1903, the Snellen double shell eye appeared commercially; it was no longer the irritating single shell sunk deep into the socket, but a revision of great ingenuity. It was light in weight and did not retain the heat of the metal eye.

32. Jeyes, P.: United States Government patent, 1892.

Snellen,[33] at the thirteenth international congress in Paris, in 1900, spoke of the glass prothesis he had developed with Müller, of Wiesbaden. He obtained his model by filling the shell eye with gypsum or gutta percha. He mentioned writing to Mr. Müller "for help in manufacturing his newly modeled prothesis." The difficulty of producing the double shell had to be surmounted, and nothing came of the work. Later, advance was made, and in 1896, after the Heidelberg Ophthalmological Congress, as he stated: "I called to see Mr. Müller, at which time we discussed the difficulty in blowing the double shell wall without breaking the globule." In September, his efforts were rewarded and the Snellen *reform Auge* (D. R. G. M. no. 107044) was produced. As a result of this new design, the sinking of the upper lid, which follows enucleation and continues to be commented on by the public in those wearing the shell eye, was corrected, and less irritation of the conjunctiva was noted. However, the design proved a failure with regard to mobility.

In the United States, Davis of New York was probably the first to design an artificial eye of glass. The Boissonneau eye in this country was first made by Pierre Gougelman. The founder of the Müller firm established its business under the names *Cartel Uri* and *Cartel Ocar*. The two cartels became one, and subsequently the most famous in Continental Europe.

Traveling ocularists today, as during Boissonneau's time, go about fitting artificial eyes. They make an artificial eye which duplicates exactly the color of the iris and design it to sit more comfortably in the socket than does the stock eye. They crack the globule to be longer in the horizontal than in the vertical direction and provide it with the same shape as that given it through the centuries (figs. 5, 6 and 7). This was done to prevent its wandering from a fixed setting. Its exact fixation provides against any desultory motion that the stump may produce.

Snellen, the great ophthalmologist of Holland, has been the only one throughout the centuries to meet the need of an artificial eye to sit forward in the socket as does the normal eye; however, he was not able to remove the *bête noire,* for today, as in ancient days, the eye is but a shield anchored in position.

It was not the ocularists alone who were at fault, but the material with which they were compelled to work, for kryolith glass, which had brought so much happiness to the afflicted in that it could be readily blown and beautifully colored, defeated the ideal the surgeon sought, namely, mobility for the prothesis. The very nature of glass, that of fragility, took it out of the hands of the person best qualified to adjust through knowledge of anatomy and physiology, the ophthalmologist himself, and placed it in the hands of persons with but a modicum of knowledge in the basic science.

The ophthalmic surgeon hardly dared touch the artificial eye for fear of breaking it. Since he did not know how to blow glass, there was nothing he could do; he had as yet no substitute products for making artificial eyes, and the material at his disposal was unalterable.

The surgeon was also at fault, for he commonly did not make a proper enucleation, nor did he grasp the teaching of Cleoburey: The socket left after enucleation is of a standard pattern; so the artificial eye is to be standardized.

THE PLASTIC ARTIFICIAL EYE

Plastics have provided an opportunity for the ophthalmologist to interest himself in a problem he has neglected, viz., his designing the prothesis instead of leaving it to those who fit artificial eyes. He neglected his responsibility when he failed to see that the prothesis is shaped so that it may move. The prothesis

33. Snellen, P.: Cong. internat. de méd., Rap. sect. d'opht. (pt. 2) **1**:27, 1900.

of the artisan was designed to thwart movement whereas the surgeon labored to make possible movement of the prothesis that thwarted motion.

The plastic eye permits alterations—it can be cut, sawed and sanded. It is not readily acted on by the tears, nor does the heat of the body affect it. It can be dropped without being broken. It may be sterilized, whereas the glass eye is a *noli me tangere.*

CONCLUSION

Historians, anatomists, physiologists, ophthalmologists, physicists and ocularists have contributed to a series of errors, which are indicated here.

Cleoburey replaces Ferrall and Bonnet in priority for the procedure of enucleation. Tenon is replaced by the ancients. The check ligaments not only hold the rectus muscles in check but act reciprocally to them. They help pull the tissues forward when the rectus muscles are cut. Besides, they function as a wedge to complete the ball and socket joint in which the eye may rotate.

The tissues of the socket come forward, particularly after an enucleation, as a result of the action of the oblique muscles the check ligaments and the elastic fibers of the capsule of Tenon. Peeling of the eye from Tenon's capsule is enucleation; nothing else is. The enucleation procedure was perfect from its first development. Imperfect procedures were the result of conjectures rather than of study of facts. The socket of enucleation is not concave.

Though the glass eye is a gem, it does not satisfy the exacting patient, who wants it set not in the rim of the bony orbit but like the orb in the orbit, so that it may move. The use of plastics solves the problem, and the ophthalmologist may now direct the making of the artificial eye of the future and see that it is properly tailored.

4325 St. Charles Street.

EFFECT OF LOCAL ANESTHETICS ON REGENERATION OF CORNEAL EPITHELIUM

MAJOR TRYGVE GUNDERSEN

AND

LIEUTENANT SUMNER D. LIEBMAN

MEDICAL CORPS, ARMY OF THE UNITED STATES

Our purpose in the present investigation was to determine experimentally the effect of various local anesthetics on the regeneration of corneal epithelium. Clinically it has been observed from time to time that local anesthetics have an inhibitory influence on the regeneration of corneal epithelium. In 1902 Fuchs,[1] for this reason, stated that patients should be prohibited from using cocaine at home for the treatment of corneal abrasions. Many of the newer anesthetics are, however, said to be innocuous. Stallard [2] stated that tetracaine has no toxic effect on the regenerating epithelium. According to Gifford,[3] 0.5 per cent butacaine sulfate or phenacaine hydrochloride causes little or no damage to the epithelium and may be used several times a day. Heretofore no attempt has been made to determine experimentally whether or not local anesthetics affect the regrowth of corneal epithelium.

METHOD

Guinea pigs (4 for the study of each drug) were used as test animals, since they are easily handled.[4] The animals were anesthetized by intraperitoneal injection of pentobarbital sodium.

The drugs used in these experiments were fresh preparations similar to those in daily use in the clinic of the Massachusetts Eye and Ear Infirmary. These drugs were solutions of 10 per cent cocaine hydrochloride, 4 per cent cocaine hydrochloride, 1 per cent butacaine sulfate, 4 per cent larocaine hydrochloride, 1 per cent phenacaine hydrochloride and 0.5 per cent tetracaine hydrochloride, all containing 0.5 per cent chlorobutanol. One per cent phenacaine hydrochloride and 0.5 per cent tetracaine hydrochloride in ointment form [5] were instilled into the right eyes of two other groups of guinea pigs. The left, or control, eyes of these animals were treated with ointment base containing no local anesthetic. The experiments for the 10 per cent cocaine hydrochloride and the 1 per cent phenacaine hydrochloride were carried out in duplicate series, and the eyes of the second series of animals were removed at varying intervals for histologic examination.

From the Howe Laboratory of Ophthalmology, Harvard University, and the Massachusetts Eye and Ear Infirmary.

Read at the annual meeting of the Massachusetts Alumni Association before the Ophthalmological Section, Boston, Jan. 21, 1942.

1. Fuchs, E.: Ueber Cocaine, Wien. klin. Wchnschr. **15**:962, 1902.

2. Stallard, H. O., in Ridley, F., and Sorsby, A.: Modern Trends in Ophthalmology, London, Butterworth & Co., Ltd., 1940, chap. 49, p. 543.

3. Gifford, S. R.: A Handbook of Ocular Therapeutics, Philadelphia, Lea & Febiger, 1942, pp. 24 and 378.

4. Cats and rabbits were also used, but the results obtained were equivocal. It was thought that the nictitating membrane interfered with equal distribution of the drug on the cornea. Identical abrasions, 2 mm. wide, were made with a metal spatula in the two eyes, from limbus to limbus, across the centers of the corneas. The lesions were immediately stained with 2 per cent fluorescein sodium to make sure that equal areas had been abraded in the two corneas. The right eye of each animal was treated with the drug under investigation every hour day and night until both eyes showed no staining or until an unequivocal result had been obtained. Usually nothing was instilled into the left eye. The corneas were stained at various intervals, as indicated on the accompanying charts, and for comparative purposes the staining areas were recorded.

5. The ointment base consisted of 3 per cent oxycholesterol in petrolatum.

Further studies were carried out to evaluate the influence of tonicity of the cocaine and the tetracaine solutions on the regeneration of corneal epithelium. Six groups of guinea pigs (4 animals in each group) were used. The right eyes of one group were treated with a 4 per cent solution of cocaine hydrochloride (hypotonic to tears). The right eyes of a second group were treated with a solution containing 4 per cent cocaine hydrochloride and 1.25 per cent sodium chloride (roughly isotonic to tears). The right eyes of a third group were treated with a solution containing 4 per cent cocaine hydrochloride and 5 per cent sodium chloride (hypertonic to tears). The remaining three groups of animals were treated in a similar manner, but 0.5 per cent tetracaine hydrochloride was substituted for 4 per cent cocaine hydrochloride. The left, or control, eyes of all the animals were treated with distilled water (hypotonic solution), 1.25 per cent sodium chloride (isotonic solution) and 5 per cent sodium chloride (hypertonic solution). All solutions contained 0.5 per cent chlorobutanol.

Since the p_H of fresh stock 4 per cent solutions of cocaine hydrochloride used in the preceding experiment was about 4, a separate study was carried out to determine whether or not the inhibitory effect was due to this relatively low p_H. The influence of the p_H alone was studied by the use of potassium acid phthalate as buffer (without an anesthetic) at p_H 2.82, 4.12 and 6.28. The effect of each solution was tested by hourly instillations into the right eyes of 3 guinea pigs. The left, or control, eyes were untreated.

The effect of each anesthetic on the intact epithelium was tested in the usual manner by hourly instillations in the eyes of normal guinea pigs.

RESULTS

The results obtained with the solutions of the various local anesthetics are summarized in the accompanying charts. The areas which stained with the fluorescein are represented in black. The dotted lines indicate the extent of the initial lesions.

Ten Per Cent Cocaine Hydrochloride.—On the third day all treated eyes showed pronounced swelling of the stroma on slit lamp examination, and on the fourth day several of the corneas presented a superficial pannus. Treatment was discontinued at this time, and the eyes of 1 animal (93) were enucleated for histologic study. Two weeks later the treated eyes of the remaining animals appeared normal except for a small, deep central corneal opacity. Obviously 10 per cent cocaine hydrochloride appreciably retarded the regeneration of epithelium (chart 1 *A*).

Four Per Cent Cocaine Hydrochloride.—The right eyes of animals in this group were treated with an aqueous solution of 4 per cent cocaine hydrochloride. Chart 1 *B* shows that the regeneration of corneal epithelium was definitely delayed by this anesthetic, although the effect was not quite so pronounced as that with the 10 per cent solution. In the treated eyes a superficial pannus did not develop, as was observed in all eyes treated with 10 per cent cocaine hydrochloride.

Effect of Variation in Tonicity of 4 Per Cent Cocaine Hydrochloride.—Chart 1 *B, C* and *D* gives the results of these studies. It can be seen that the inhibitory effect diminished as increasingly hypertonic solutions were used.

Tetracaine Hydrochloride, 0.5 Per Cent.—This anesthetic was studied in the same manner as was 4 per cent cocaine hydrochloride, with results which, as can be seen in chart 2 A, were qualitatively similar. The inhibitory effect on the regeneration of epithelium, while not so striking as that of cocaine, was nevertheless present.

Effect of Variation in Tonicity of 0.5 Per Cent Tetracaine Hydrochloride.—Chart 2 *A, B* and *C* shows that with increasing tonicity the inhibitory effect of 0.5 per cent tetracaine hydrochloride was almost eliminated.

Other Anesthetics.—The delayed healing of the epithelium was observed in varying degrees with 1 per cent phenacaine hydrochloride, 1 per cent butacaine sulfate and 4 per cent larocaine hydrochloride (chart 2 *D, E* and *F*). As can be seen in these portions of the chart, 1 per cent phenacaine hydrochloride and 0.5 per cent tetracaine hydrochloride were the least toxic to the regenerating epi-

thelium. One per cent butacaine sulfate, 4 per cent larocaine hydrochloride, 4 per cent cocaine hydrochloride and 1 per cent cocaine hydrochloride showed an increasingly inhibitory effect, in the order named. Five-tenths per cent tetracaine hydrochloride and 1 per cent phenacaine hydrochloride in ointment base gave results similar to those of aqueous solutions of these drugs, and the data are not included.

Effect of the p_H.—It was found that the solution which buffered at a p_H of 2.82 with no anesthetic had a definite inhibitory effect on the regeneration of the corneal

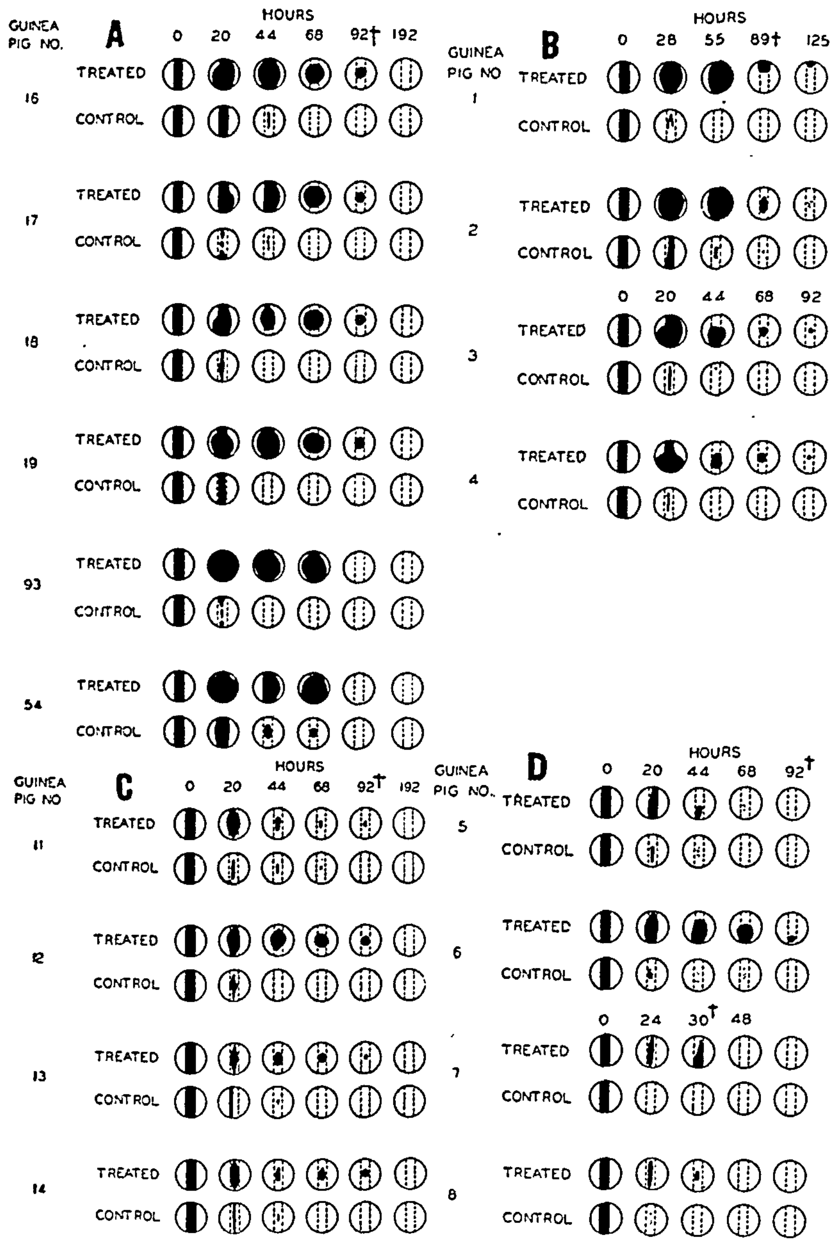

Chart 1.—Effects of 10 and 4 per cent cocaine hydrochloride on the regeneration of corneal epithelium. The areas which stained with fluorescein are represented in black. The dagger (†) indicates the time at which treatment was discontinued. *A* represents results with 10 per cent cocaine hydrochloride; *B,* with 4 per cent cocaine hydrochloride in hypotonic solution of sodium chloride; *C,* with 4 per cent cocaine hydrochloride in isotonic solution of sodium chloride, and *D,* with 4 per cent cocaine hydrochloride in hypertonic solution of sodium chloride.

epithelium, whereas the solutions with a p_H of 4.12 and 6.28 had no effect. None of the anesthetic solutions used had a p_H of less than 4 when freshly prepared. Moreover, the anesthetic solutions used in the aforedescribed experiments were not buffered and probably became somewhat less acid when brought into contact with

the cornea and tears. It is concluded, therefore, that the aforedescribed results were not dependent on the p_H of the solutions.

Effect of Local Anesthetics on Intact Epithelium.—Ten and 4 per cent solutions of cocaine hydrochloride instilled hourly into the intact eyes of guinea pigs produced areas on the corneas which stained with fluorescein. The other anesthetics did not produce staining areas.

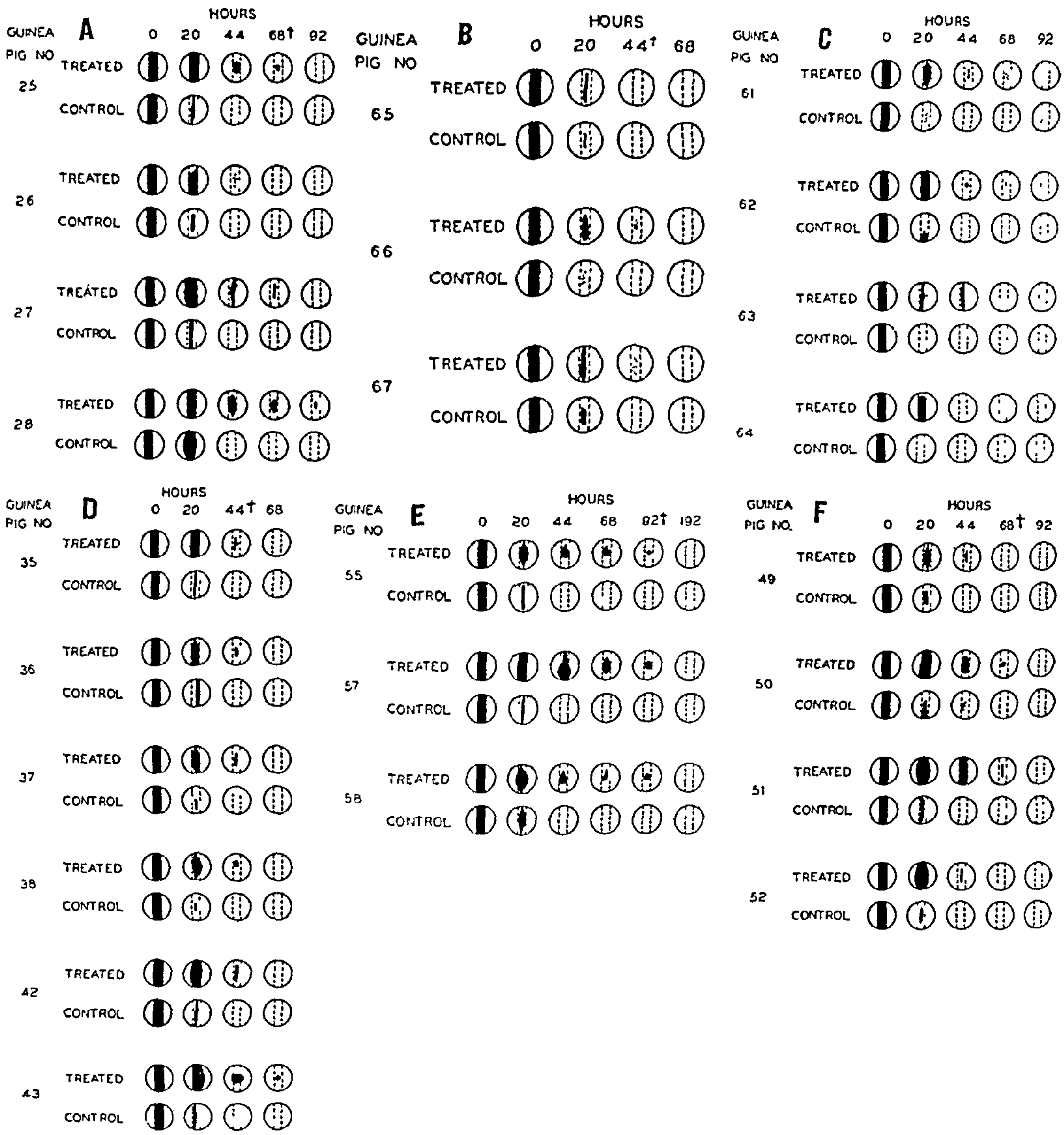

Chart 2.—Effect of 0.5 per cent tetracaine hydrochloride and various other local anesthetics on the regeneration of corneal epithelium. The method of recording is the same as that used in chart 1. *A* represents results with 0.5 per cent tetracaine hydrochloride in hypotonic solution of sodium chloride; *B*, with 0.5 per cent tetracaine hydrochloride in isotonic solution of sodium chloride; *C*, with 0.5 per cent tetracaine hydrochloride in hypertonic solution of sodium chloride; *D*, with 1.5 per cent phenacaine hydrochloride; *E*, with 4 per cent larocaine hydrochloride, and *F*, with 1 per cent butacaine sulfate.

Pathologic Studies.—Pathologic studies were made on two groups of animals, one treated with 10 per cent cocaine hydrochloride and the other with 1 per cent phenacaine hydrochloride. The eyes were sectioned perpendicular to the long axis

of the abrasion, and the control eyes, or left, were compared with the treated eyes. The latter showed loss of cellular boundaries, with pale, swollen nuclei in the cells which bounded the abrasion. These differences were progressively more pronounced in the animals which had received longer treatment. Mitotic figures were difficult to find in either the treated or the control eyes. The epithelium bounding the abrasions in the untreated eyes looked more normal, having visible cell boundaries and nuclei. In some of the eyes treated with 10 per cent cocaine hydrochloride there were leukocytic infiltration of the stroma and polymorphonuclear cells on the endothelium and in the anterior chamber. The series treated with phenacaine showed no such inflammatory reaction, although there were varying degrees of swelling of the corneal stroma beneath the abrasions.

SUMMARY

It can be seen from the results described that all of the local anesthetics tested had some delaying effect on the healing process of the corneal epithelium of the guinea pig. This effect is modified in degree by the concentration and the tonicity of the anesthetic agent. The p_H is probably not a determining factor, since buffered solutions at a p_H comparable to that of the anesthetics used showed relatively little inhibitory action. Of the various anesthetics tested, 1 per cent phenacaine hydrochloride and a hypertonic 0.5 per cent solution of tetracaine hydrochloride were the least toxic to the regenerating epithelium.

243 Charles Street, Boston.

BINOCULAR REFRACTION WITH CROSS CYLINDER TECHNIC

MAJOR H. SAUL SUGAR
MEDICAL CORPS, ARMY OF THE UNITED STATES

It is a well known fact that many persons who wear corrective lenses the prescription for which has been determined by accurate monocular refraction and who do not have abnormal lateral or vertical phorias are uncomfortable during binocular vision. In many cases the trouble is due to changes in the axes of cylinders when both eyes are used together for distant vision and during convergence accommodation. Several test methods have been devised to determine these changes; yet no cases were reported prior to those of Hughes,[1] in 1941. It is the purpose of this paper to analyze the changes in the axis of astigmatism under varying conditions in a small series of 70 normal eyes with astigmatism of 1.00 D. or more and to introduce the use of the cross cylinder to determine these changes under binocular fixation. All these eyes were those of patients with binocular single vision. As shown in the table, the axes were determined monocularly during and after cycloplegia for 20 feet (6 meters) and binocularly for both 20 feet and 10 inches (25 cm.). In all instances the changes were checked several times to minimize errors. Thirty-three of the 70 eyes had some changes in axis. Twenty-four varied in monocular axis during and after cycloplegia. Only 4 showed variations between the monocular and the binocular axis at 20 feet. Fourteen eyes had changes between the binocular axis at 20 feet and that at 10 inches.

The cause of the shift in axis under varying conditions has been discussed extensively. The shift from the cycloplegic to the postcycloplegic monocular axis for fixation at 20 feet may be explained by slight changes in the position of the crystalline lens. It has been suggested that the shift may be due to aberrations produced by the outer zone of the cornea when the pupil is dilated. That this is untrue was suggested by the fact that the axis did not change when a disk with a hole 3.5 mm. in diameter was placed behind the lenses in the trial frame. The change from monocular to binocular conditions and the changes associated with convergence accommodation are not as easily explained. Four theories have been advanced. The first is that lenticular changes cause the shift in the axis. Hughes, in a report of 4 cases in which the axis of astigmatism changed on accommodation, concluded that "the change in axis could not be due to rotation of the eye as a whole, as no abnormal tension was seen with the unaided eye, with the microscope or with the ophthalmometer. The phenomenon must therefore be lenticular in origin." The second theory is that a fusional compensation occurs (Verhoeff[2]), which results in a slight shift in axis. The third theory is that of torsional movements of the globe (cyclophoria). This has been championed by Savage. A fourth theory, advanced by Pascal,[3] is that the action of the extrinsic muscles in near vision slightly changes the curves of the cornea.

From the Eye Clinic, Barnes General Hospital, Vancouver, Wash.

1. Hughes, W. L.: Change of Axis of Astigmatism on Accommodation, Arch. Ophth. **26**:742 (Nov.) 1941.
2. Verhoeff, F. H.: Description of a Reflecting Phorometer, Am. J. Physiol. Optics **7**:39, 1926.
3. Pascal, J. I.: The Axis of Astigmatism, Arch. Ophth. **27**:189 (Jan.) 1942.

As a result of the observations in the present series of cases, it appears that each theory may have its place in the explanation of the various shifts. Change in position of the lens most reasonably explains the difference in the monocular axes during and after cycloplegia. Fusional compensations may explain the change in axis from monocular to binocular conditions when the subject is fixing at 20 feet. The change in axis from distance to near vision during binocular fixation appears to be most reasonably explained by torsional changes. That this is at least possible is suggested by the observations in a case of persistent postoperative paradoxic diplopia with horror fusionis. A soldier aged 23 had begun to show squint at the age of 22 months. In 1936 the squint was corrected surgically, but diplopia resulted. He was able to tolerate the diplopia with a correction of 3 prism diopters base in before each eye, 2 prism diopters base up before the right eye and 2 prism diopters base down before the left eye. The images were then as close together as possible. For near vision, however, the prisms had to be rotated nasalward, 82 and 172 degrees for the right eye and 107 and 17 degrees for the left eye in order to make the patient comfortable.

Changes in Axis of Cylinders

				20 Feet (6 Meters)			10 Inches (25 Cm.)
Case No.	Age, Yr.	Right or Left Eye	Strength of Cylinder	Axis Under Cycloplegia	Monocular Axis, Post-cycloplegic	Binocular Axis, Post-cycloplegic	Binocular Axis, Near Vision
1	34	R	+1.12	110	117	117	120
2	24	R	+1.50	170	170	170	175
3	24	L	+1.50	10	10	10	5
4	23	R	+2.00	100	100	100	95
5	24	R	+1.12	90	87	87	87
6	24	L	+1.00	90	87	87	87
7	25	R	+1.00	140	140	140	135
8	41	R	+1.00	...	110	110	115
9	37	R	+2.00	107	107	107	102
10	44	R	+1.25	85	88	85	90
11	32	R	+1.50	15	10	10	10
12	29	L	+1.12	65	50	50	50
13	30	L	+1.12	97	100	100	100
14	43	L	+1.25	..	145	145	140
15	24	R	+2.50	110	110	110	115
16	24	L	+1.50	53	57	57	57
17	20	R	+2.00	100	95	95	95
18	20	L	+1.62	80	75	75	75
19	21	R	+1.25	105	114	114	114
20	30	R	+1.37	172	165	165	165
21	30	L	+1.87	160	165	165	165
22	28	R	+1.75	100	105	105	105
23	28	L	+1.00	65	65	65	70
24	38	L	+2.00	80	86	86	86
25	30	R	+1.75	115	110	110	110
26	41	R	+2.75	116	110	110	110
27	22	L	+2.00	90	95	95	95
28	21	R	+2.00	90	75	75	75
29	40	R	+3.50	177	5	180	180
30	22	R	+1.25	35	35	30	35
31	24	L	+1.00	77	82	82	82
32	44	R	+1.37	47	43	47	52
33	44	L	+1.00	150	155	155	160

Of the many methods [4] which have previously been used to determine the astigmatic axis under binocular fixation, some require special apparatus, such as the Leland refractor,[5] which uses polaroid filters, while another utilizes two separate charts with a long septum between them, placed so that each eye of the patient sees a separate chart. One may use a neutral density filter or a + 2.00 D. sphere (Copeland) or a multiple pinhole disk before the eye not being tested. Still

4. Copeland, J. C.: Locating the Astigmatic Axis Under Binocular Fixation, in Ten Years of Optical Developments (November 1940), Chicago, Riggs Optical Company, 1942.

5. van Wien, S.: The Leland Refractor: Method for Refraction Under Binocular Conditions, Arch. Ophth. **23**:104 (Jan.) 1940.

another test is based on dissociation of a single line of test letters with a 6 D. vertical prism. The objection to the latter tests is that there is definite dissociation of the two eyes and true binocular function is not tested.

For the past four years I have used the cross cylinder (+ 0.25 D.; — 0.25 D.) for determination of the axis of cylinders binocularly for distance, and more recently I have employed it to determine the axis of astigmatism binocularly for near vision when reading glasses alone were ordered. In explaining the method I shall first discuss briefly my refractive procedure with cycloplegia and at the postcycloplegic examination.

After careful retinoscopy with cycloplegia, plus cylinders only being used, the lenses representing the net retinoscopic findings are placed in the trial frame, with the eye not under examination covered. The spherical correction is modified as necessary, the smallest test letters visible, usually the 20/20 line, being used. Frequently when a small amount of residual accommodation is present, the patient prefers the addition of a — 0.25 D. sphere. If another + 0.25 D. sphere is held before the lens combination and the patient prefers it, the — 0.25 D. sphere was accommodative and should be removed. When the best spherical correction has been obtained, the axis of the cylindric correction is determined with the cross cylinder. The 20/50 or the 20/70 test letters are now used. The details of the use of the cross cylinder for axis and strength have been well described by Crisp [6] and others.

The strength of the cylinder in the trial frame is modified by placing the plus and minus axes of the cross cylinder alternately in front of the trial case cylinder with the axes parallel. The cross cylinder indicates not the amount of cylinder to be added or subtracted but only the direction of change. Changes of 0.12 D. are used. If a + 1.00 D. cylinder is in the trial frame at axis 90 and more letters are seen, or are better seen, with the minus position of the crossed cylinder, a — 0.12 D. cylinder is added to the cylinder in the frame. The cross cylinder is again placed alternately in the minus and in the plus position before the lens, and the best position is determined. If the plus position is favored, the correct cylinder is one between + 0.87 and + 1.00 D. The one preferred by the patient is to be used. It is usually the former. To be certain, the simple cylinders alone with 20/20 or 20/15 test letters are again used. If the minus position is favored, another — 0.12 D. cylinder is added until the plus position is favored. If a + 1.00 D. cylinder is in the trial frame at axis 90 and more letters are seen with the plus position of the cross cylinder, a + 0.12 D. cylinder is added to the cylinder in the frame. The cross cylinder is again used, and the favored position is determined, whether plus or minus. If the minus position is favored, the correct cylinder is one between + 1.00 and + 1.12 D. The former is usually ordered. If the plus position is favored, another + 0.12 D. cylinder is added until the minus position is favored.

When the correct strength and axis of the cylinder are determined, the smallest visible test letters are again used, usually the 20/20 or the 20/15 line. Changes in the sphere are now made. Changes of 0.12 D. should be made where recognized.

The same procedure is carried out monocularly for the other eye.

At the postcycloplegic examination all testing is done binocularly. First, the total sphere is reduced equally as necessary or as indicated. Then the cross cylinder test for axis should be made first on one eye and then the other, with

6. Crisp, W. H.: The Cross-Cylinder Tests Especially in Relation to the Astigmatism Axis, Tr. Ophth. Soc. U. Kingdom 60:495, 1931.

the patient using both eyes. No attempt is made to suspend the vision of the eye which is not under refraction. In cases in which spectacles with high cylinders are ordered for near vision only, the same procedure should be used for the axis of each cylinder, with both eyes open, the patient fixing on test material in the position of ordinary reading. The smallest Snellen and Jaeger test types must be used for distance and near vision respectively. The strength of cylinder is not usually changed except when glasses are ordered for the first time in cases of high cylindric errors and in cases of anisometropia, conical cornea, corneal opacities or eccentric pupil.

When manifest refractions are made with the cross cylinder, the best sphere must be determined before cylindric changes are made, as was pointed out by Jackson.[7] Recently Williamson-Noble[8] showed that if a patient is fogged he tends to choose too strong a cylinder against the rule, whereas in the opposite condition, when hyperopia is undercorrected or myopia is overcorrected, he tends to choose too strong a cylinder with the rule. This is based on the fact that blurred letters are more easily recognized when their vertical components are in better focus then when the horizontal ones are clearer. Copeland[9] expressed the belief that the use of the cross cylinder under a slight fog leads to fallacious results, since the dioptric midpoint is moved and symmetric comparison is lost when pivoting around the false midpoint.

After the best sphere is determined in manifest refraction, the cross cylinder is first used in the 90 and in the 180 axis, and either plus or minus cylinder is added, in the indicated axis. Individual preference must be considered as to whether a plus or a minus cylinder is used. As soon as a 0.25 D. cylinder is found, the axis is determined as previously described, and further changes in axis strength are made. When the total astigmatic correction has been found, the axis should be rechecked. If any amount of cylinder is found, the sphere must be changed in an amount equal to half the cylinder and opposite it in sign. It should be changed with each 0.25 or 0.5 D. of cylinder. If + 0.25 D. of cylinder is added, half this amount, or 0.12 D., should be subtracted from the sphere. In many cases in which a considerable amount of cylinder is present, the changes in sphere may be made with each 0.5 D. of change in cylinder and the 0.12 D. sph. changes made at the end point. This procedure follows the principle of spherical equivalents. Because this principle is important in cross cylinder refraction, and also in the obtaining of comfortable binocular vision in cases of anisometropia, a brief résumé of its use in the latter will not be amiss. Copeland[10] introduced this principle in 1928. It had been employed by designers of ophthalmic lenses in attempts to establish the correct base curve for the reduction of marginal astigmatism in compound lenses. In the ophthalmologic journals the subject has been discussed only by Prangen.[11]

The spherical equivalent of a compound lens system is located at the midpoint between the two principal meridians of the lens system. In other words, it is

7. Jackson, E.: How to Use the Cross Cylinder, Am. J. Ophth. **13**:321, 1930.

8. Williamson-Noble, F. A.: Possible Fallacy in the Use of the Cross-Cylinder, Brit. J. Ophth. **27**:1, 1943.

9. Copeland, J. C.: Personal communication to the author.

10. Copeland, J. C.: A Study in the Application of Cylindric Corrections, Optom. Weekly **19**:191 (April 5) 1928; in Ten Years of Optical Development, Chicago, Riggs Optical Company, 1942: An Important Diagnostic Point in the Correction of Astigmatism, May-June 1931; Analysis and Use of the Crossed Cylinder, September 1931.

11. Prangen, A. de H.: The Significance of Sturm's Interval in Refraction, Am. J. Ophth. **24**:413, 1941; Some Problems and Procedures in Refraction, Arch. Ophth. **18**:432 (Sept.) 1937.

the circle of least confusion located at the dioptric midpoint of the interval of Sturm. The term "spherical equivalent" is somewhat loosely used. Perhaps the terms "spherical mean" or "spherical average" would be better.[9] Numerically, the spherical equivalent of a compound lens system is equal to the spherical power of the system plus half the power of the cylinder. The spherical equivalent of a simple cylinder is equal to half the power of the cylinder. The following cases exemplify the principle.

Case 1.—Private E. W., aged 23 (chart 1).

Refraction with 5 per cent homatropine hydrobromide cycloplegia gave the following results:

Right eye: —2.75 D. sph. ⊃ + 2.00 D. cyl., axis 100
Left eye: — 1.50 D. sph. ⊃ + 0.25 D. cyl., axis 90

At postcycloplegic examination this correction gave normal visual acuity of 20/20 for each eye, but caused severe discomfort binocularly.

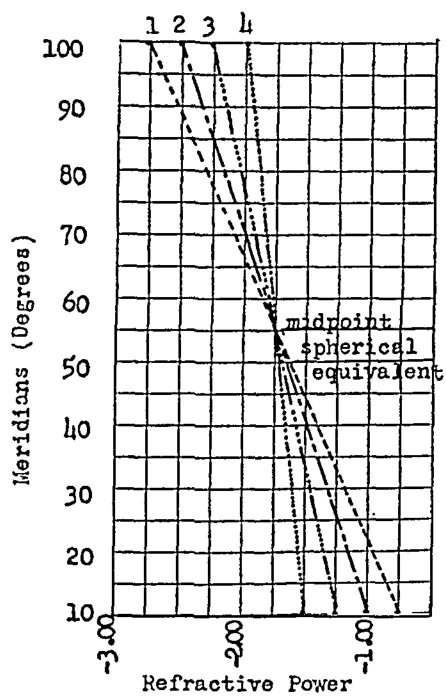

Chart 1.—Schematic representation of lens combinations with the same spherical equivalent as that used in case 1. Combination 3 was preferred.

1. —2.75 D. sph. ⊃ + 2.00 D. cyl., axis 100 (full correction)
2. —2.50 D. sph. ⊃ + 1.50 D. cyl., axis 100
3. —2.25 D. sph. ⊃ + 1.00 D. cyl., axis 100
4. —2.25 D. sph. ⊃ + 0.50 D. cyl., axis 100

The spherical equivalent rule was used to determine the various lens combinations that could be used for the right eye without disturbance of the position of the optical midpoint, as shown in chart 1. The rule is as follows: In reduction of a cylinder, half the reduced amount is added to the sphere, the sign of the cylinder being maintained during the addition.

1. —2.75 D. sph. ⊃ + 2.00 D. cyl., axis 100 (full correction)
2. —2.50 D. sph. ⊃ + 1.50 D. cyl., axis 100
3. —2.25 D. sph. ⊃ + 1.00 D. cyl., axis 100 (preferred)
4. —2.00 D. sph. ⊃ + 0.50 D. cyl., axis 100

These combinations were tried in the order listed, beginning with the stronger cylinders. The patient can easily tell whether the combination is comfortable within a few minutes. The most comfortable combination may be tried in a trial frame in the waiting room for a

half-hour as a test. In this particular case the third combination gave comfort and was prescribed. Visual acuity with this system was 20/25.

CASE 2.—Private J. D. N., aged 21 (chart 2).

Refraction with 5 per cent homatropine hydrobromide cycloplegia gave the following results:

Right eye: —4.00 D. sph. ⊃ + 2.75 D. cyl., axis 110
Left eye: —0.50 D. sph. ⊃ + 1.00 D. cyl., axis 90

The lens combinations tried were:

1. —4.00 D. sph. ⊃ + 2.75 D. cyl., axis 100 (full correction)
2. —3.75 D. sph. ⊃ + 2.25 D. cyl., axis 100
3. —3.50 D. sph. ⊃ + 1.75 D. cyl., axis 100
4. —3.00 D. sph. ⊃ + 1.25 D. cyl., axis 100 (preferred)
5. —2.75 D. sph. ⊃ + 0.75 D. cyl., axis 100

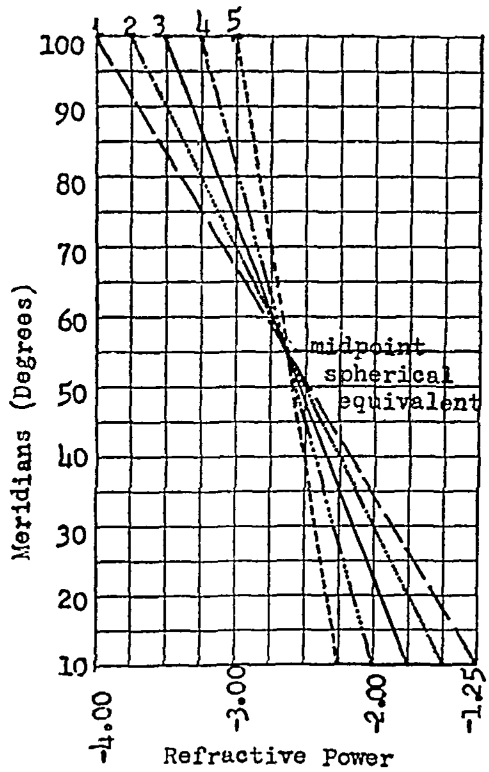

Chart 2.—Schematic representation of lens combinations with the same spherical equivalent as that used in case 2. Combination 4 was preferred.

1. —4.00 D. sph. ⊃ + 2.75 D. cyl., axis 100 (full correction)
2. —3.75 D. sph. ⊃ + 2.25 D. cyl., axis 100
3. —3.50 D. sph. ⊃ + 1.75 D. cyl., axis 100
4. —3.25 D. sph. ⊃ + 1.25 D. cyl., axis 100
5. —3.00 D. sph. ⊃ + 0.75 D. cyl., axis 100

The prescription preferred was:

Right eye: —3.00 D. sph. ⊃ + 1.25 D. cyl., axis 100
Left eye: —0.50 D. sph. ⊃ + 1.00 D. cyl., axis 90

CASE 3.—Private G. W. A., aged 28 (chart 3).

Refraction with 5 per cent homatropine hydrobromide cycloplegia gave the following results:

Right eye: + 4.00 D. sph. ⊃ + 1.00 D. cyl., axis 95 (20/20 vision)
Left eye: + 3.00 D. sph. ⊃ + 3.25 D. cyl., axis 75 (20/20 vision)

Sphere cut for each eye was + 1.75 D.

The lens combinations tried with the left eye were as follows:

1. + 1.25 D. sph. ⊂ + 3.25 D. cyl., axis 75
2. + 1.50 D. sph. ⊂ + 2.75 D. cyl., axis 75
3. + 1.75 D. sph. ⊂ + 2.25 D. cyl., axis 75
4. + 2.00 D. sph. ⊂ + 1.75 D. cyl., axis 75 (preferred)
5. + 2.25 D. sph. ⊂ + 1.25 D. cyl., axis 75

The prescription preferred was:

Right eye: + 2.25 D. sph. ⊂ + 1.00 D. cyl., axis 95
Left eye: + 2.00 D. sph. ⊂ + 1.75 D. cyl., axis 75

Case 4.—Private B. B. I., aged 20 (chart 4).

Refraction with 5 per cent homatropine hydrobromide cycloplegia gave the following results:

Right eye: + 1.50 D. sph., axis 90
Left eye: — 2.50 D. sph. ⊂ + 3.50 D. cyl., axis 105

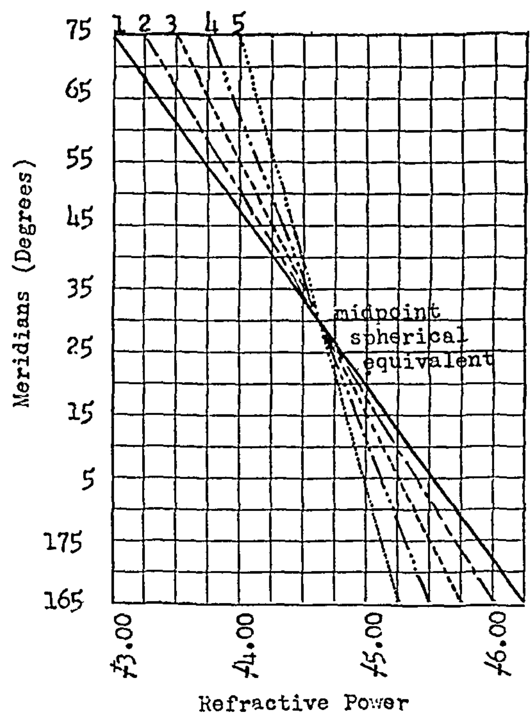

Chart 3.—Schematic representation of lens combinations with the same spherical equivalent as that used in case 3. Combination 4 was preferred.

1. + 3.00 D. sph. ⊂ + 3.25 D. cyl., axis 75 (full correction)
2. + 3.25 D. sph. ⊂ + 2.75 D. cyl., axis 75
3. + 3.50 D. sph. ⊂ + 2.25 D. cyl., axis 75
4. + 3.75 D. sph. ⊂ + 1.75 D. cyl., axis 75
5. + 4.00 D. sph. ⊂ + 1.25 D. cyl., axis 75

The lens combinations tried with the left eye were as follows:

1. — 2.50 D. sph. ⊂ + 3.50 D. cyl., axis 105 (full correction)
2. — 2.25 D. sph. ⊂ + 3.00 D. cyl., axis 105
3. — 2.00 D. sph. ⊂ + 2.50 D. cyl., axis 105
4. — 1.75 D. sph. ⊂ + 2.00 D. cyl., axis 105 (preferred)
5. — 1.50 D. sph. ⊂ + 1.50 D. cyl., axis 105
6. — 1.25 D. sph. ⊂ + 1.00 D. cyl., axis 105

The prescription preferred was:

Right eye: + 1.50 D. sph., axis 90
Left eye: — 1.75 D. sph. ⊂ + 2.00 D. cyl., axis 105

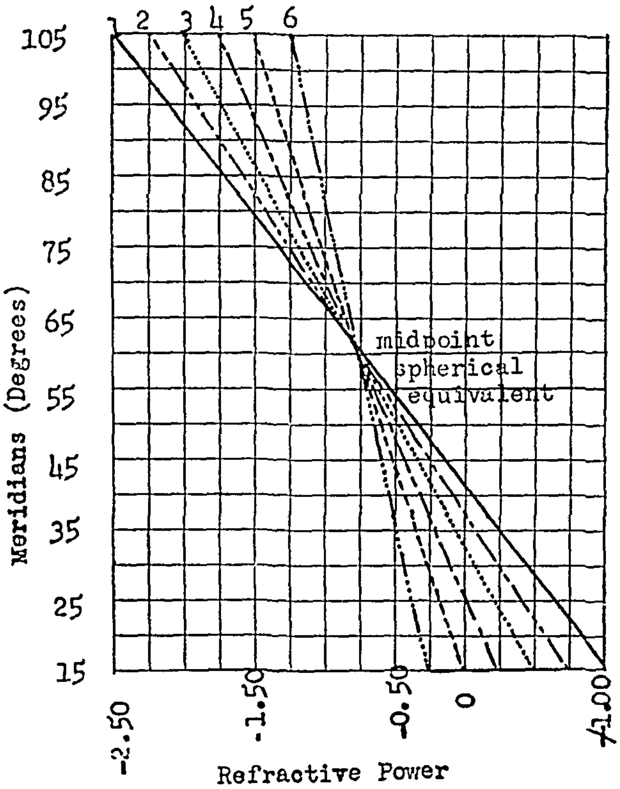

Chart 4.—Schematic representation of lens combinations with the *same spherical equivalents* as that used in case 4. Combination 4 was preferred.

1. —2.50 D. sph. ⊃ + 3.50 D. cyl., axis 105 (full correction)
2. —2.25 D. sph. ⊃ + 3.00 D. cyl., axis 105
3. —2.00 D. sph. ⊃ + 2.50 D. cyl., axis 105
4. —1.75 D. sph. ⊃ + 2.00 D. cyl., axis 105
5. —1.50 D. sph. ⊃ + 1.50 D. cyl., axis 105
6. —1.25 D. sph. ⊃ + 1.00 D. cyl., axis 105

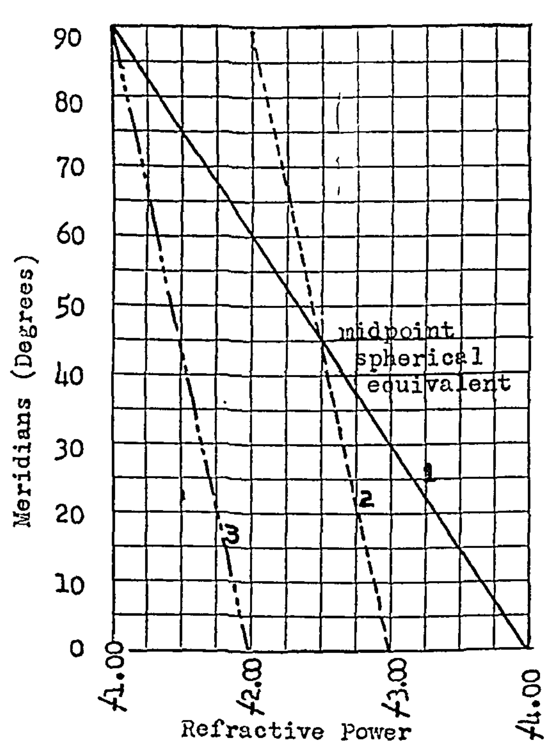

Chart 5.—Schematic representation of the spherical equivalent as compared with the simple reduction of cylinder for a patient with full correction. The full correction, + 1.00 D. sph. ⊃ + 3.00 D. cyl., axis 90, is indicated by line *1;* the spherical equivalent, + 2.00 D. sph. ⊃ + 1.00 D. cyl., axis 90 (reduction of cylinder with proportionate increase of sphere), by line 2, and the simple reduction of cylinder without change in the sphere, + 1.00 D. sph. ⊃ + 1.00 D. cyl., axis 90, by line *3.*

The value of the cross cylinder in determination of cylinder strength depends on the fact that it does not interfere with the "spherical equivalent" value but changes the sphere and the cylinder in the correct proportions. When a simple cylinder is added to any lens system, however, the optical midpoint is changed, and the "spherical equivalent" value is altered, as shown in chart 5.

CONCLUSIONS

Because of changes in the axis of astigmatism under various monocular and binocular conditions, the final prescription for correction of lenses should be based on testing under binocular fixation. The use of the cross cylinder is advocated as a simple method for such testing. The principle of "spherical equivalents" should be considered in binocular refraction, especially manifest refraction, and in determination of a comfortable binocular prescription in cases of anisometropia.

Mr. J. C. Copeland, of Riggs Optical Company, introduced the principle of spherical equivalents to the residents at the Illinois Eye and Ear Infirmary, Chicago.

A PROBLEM OF SPLIT MACULA

STUDY OF THE VISUAL FIELDS

JOHN N. EVANS, M.D.
AND
JEFFERSON BROWDER, M.D.
BROOKLYN

The course and function of various fasciculi of the optic pathway have held the interest of ophthalmologists and neuroanatomists for many generations because knowledge in this field has a broad application to the diagnosis and treatment of ocular and cerebral disease. There are two general avenues of approach for studies of these fiber bundles. One may produce experimental lesions in various laboratory animals and study the resulting progress of fiber degeneration, or one may make functional studies on human beings who are suffering from certain localized lesions. The difficulties in making functional studies on the visual apparatus of even the subhuman primates are such that one cannot relate degenerative lesions to specific functional defects. For instance, accurate studies of visual acuity and visual fields are necessary to identify the defects caused by the damage to a particular group of fibers. It is recognized that such studies cannot be made on laboratory animals.

Functional studies made on human subjects can be supported by anatomic evidence only when the injury or disease is observed at autopsy or operation. Such primary damage must be so restricted and so located as to exclude secondary involvement of adjacent structures which might give rise to disturbances confusing the picture of the primary lesion. Seldom, if ever, is there opportunity to observe the effects of focal lesions which have been produced under ideal conditions. During World War I minute fragments of missiles on occasion penetrated the brains of soldiers and produced restricted lesions of the cortex and the fiber pathways. The resulting clinical signs were investigated by workers in various warring countries. Their studies arrived at closely similar conclusions.[1] It is obvious, however, that these war injuries may have been complicated by infection, hemorrhage or other damage sustained at the same time. Such material is acceptable only because similar studies by many independent workers supplied data which, when interpreted, forced the same conclusions.

When the presented case of craniopharyngioma afforded an opportunity for special study, it was realized that any evidence derived could be accepted only as part of a general pattern. Investigation of this case seemed especially worth while since no similar studies are recorded in the literature. A review of the literature disclosed but 2 instances in which the optic chiasm was split anteroposteriorly. In 1930 Cushing[2] referred to 2 such cases in his classic paper on the chiasmal syndrome. Haden[3] apparently reported the latter of these cases (that of Miss

Read at the Seventy-Ninth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 11, 1943.

1. Horrax, G.: Contributions of the War to the Physiology of the Nervous System, Physiol. Rev. **1**:269, 1921.

2. Cushing, H.: The Chiasmal Syndrome, Arch. Ophth. **3**:505 (May); 704 (June) 1930.

3. Haden, H. C.: Studies of the Changes in the Optic Discs, Visual Fields, and Vision Following Bisection of the Optic Chiasm, Tr. Am. Ophth. Soc. **34**:208, 1936.

Betty E.) again in 1936. He had originally referred the patient to Cushing in 1929. Unfortunately, the postoperative studies of the central visual fields in these reports do not supply sufficiently detailed data for comparison with the case here presented. The amount of postoperative vision in Cushing's first case was not actually stated, but the patient was apparently able to read. The best vision in the second, or the Haden-Cushing, case was 6/30 in the right eye and 6/7 to 6/6 (questionable) in the left eye. No reference is made to the correcting glass in either report. It will become evident that these reports are not useful for comparison with data in the present study.

STATEMENT OF THE SURGICAL PROBLEM

The major therapeutic problem that presents itself in an attempted removal of a craniopharyngioma is minimal injury to the hypothalamic nuclei and their connecting pathways. Toward this end three methods of surgical approach were utilized: first, removal of the tumor piecemeal, the optic apparatus being left intact; second, section of the one optic nerve in order to obtain a better exposure of that part of the tumor situated beneath the chiasm, and, third, splitting of the optic chiasm and division of the anterior communicating artery. In the case herein recorded the third procedure was followed.

REPORT OF A CASE

History.—W. M., a 13 year old schoolboy, was admitted in a stuporous state to the Brooklyn Hospital on April 15, 1939. The following notations from the history are pertinent. The middle of 1938 marked the onset of vague headaches, and on rare occasions these attacks were associated with vomiting. During the early part of 1939 the child's interest in schoolwork slackened somewhat. The attacks of headache and vomiting became more frequent, and there was progressive, slight loss of weight. On April 4, 1939, while he was swimming, he asked his brother-in-law to help him from the pool, and immediately the extremities became stiff and the fingers were clenched over the thumbs. The attack was of short duration, and immediate recovery was sufficiently complete for him to dress and go home by subway. On his arriving home there were vomiting and headache, both of which continued at irregular intervals for the next ten days. Also, during this period, there were occasional transitory attacks of generalized rigidity with loss of consciousness. On April 14, the day before his admission to the hospital, the attacks of rigidity became so frequent that he scarcely recovered from one before another occurred. Finally, a continuous state of stupor supervened, accompanied by periodic spells of transitory rigidity and apnea.

Examination.—On his entry to the hospital, examination disclosed flaccid extremities. However, every fifteen or twenty minutes a decerebrate type of convulsion occurred, lasting from one to two minutes, during which all the extremities were held in extension. The face was pale; the lips were cyanotic, and the skin over the trunk was dusky and mottled. The extremities showed a pronounced bluish red mottling; they were cold, and the nails were cyanotic. The pulsations of the peripheral arteries were not palpable. The blood pressure was not obtainable in either the arm or the thigh. The heart rate was 160 per minute. The temperature was 99.8 F. by rectum. After the application of painful stimuli, the patient would rouse sufficiently to push the examiner's hand away and mumble a few unintelligible words. The body contour was characteristic of the Fröhlich syndrome. The pupils were small and did not react to light. Papilledema was present, the elevation being 2 D. in the right eye and 1 D. in the left eye. Paresis of supranuclear origin was demonstrable on the right side of the face. The deep reflexes were not obtained. The abdominal and cremasteric reflexes were present bilaterally but were readily exhausted. The Babinski sign was demonstrable on both sides. Pinprick over all parts of the body evoked facial grimaces and withdrawal of the part stimulated. The red blood cells numbered 7,750,000 and the white blood cells 39,400, with 95 per cent polymorphonuclear leukocytes.

Operation.—It was decided to perform a ventriculographic examination, followed by ventricular drainage by means of a catheter introduced into one of the lateral ventricles. Two hours after admission bilateral postparietal cranial burr holes were made, and the ventricular fluid was completely replaced with air. Roentgenograms disclosed pronounced dilatation of

both lateral ventricles, absence of air in the third and fourth ventricles and a calcific deposit in the suprasellar region, with distortion of the bony outline of the sella turcica. After ventricular drainage there was some improvement in that the patient obeyed simple commands and spoke spontaneously, although somewhat facetiously. The cutaneous cyanosis, the tachycardia (rate 160 to 210 per minute) and the absence of a recordable blood pressure persisted. During the ensuing four days his condition was sufficiently improved to permit further operative measures. On April 19, with use of local anesthesia, a small right frontal bone flap was outlined and turned; the lateral ventricle was tapped, and the chiasmal area was easily identified by elevation of the frontal lobe. A suprasellar cyst was exposed, widely opened and irrigated. The operator not being satisfied that this procedure had relieved the obstruction of the cerebrospinal fluid pathways, the anterior part of the right lateral ventricle was entered, and a blue-domed cystic structure was visualized through an enlarged foramen of Monro. It was determined that this represented the posterior aspect of the aforementioned cyst. The wound was closed, and a transfusion of 300 cc. of citrated blood was administered. The systolic blood pressure was now recorded as 70 mm. of mercury.

Postoperative Course.—Improvement was prompt in every respect, and within three days after the operation the patient was interested in his surroundings and talked intelligently. The peripheral mottling and cyanosis slowly disappeared, and the systolic blood pressure was maintained at 80 to 90 mm. of mercury. No abnormalities of water metabolism were demonstrable. Attempted perimetric examination, on May 6, was not satisfactory, although one could conclude with fair certainty that vision in the temporal fields for 5 mm. white test objects at 330 mm. was not impaired. The patient was discharged from the hospital on May 10. Examination six months later disclosed slight pallor of the optic nerve heads, no defects in the visual fields, a gain in weight of 23 pounds (10.4 Kg.) and normal cellular constituents of the peripheral blood. He returned to school and did well in his studies until about the middle of January 1940. At this time the appetite became poor, and he began to lose weight. During February 1940 he was inattentive in school, complained of headaches and occasionlly vomited. He exhibited irritability, restlessness and periods of listlessness, until his second admission to the hospital, on March 2, 1940. The body contour showed no appreciable change. The optic nerve heads were pale but well outlined. No defect of the visual fields for white was detected. The cytologic constituents of the blood were normal.

Second Operation.—In view of the technical difficulties encountered in previous cases in which complete removal of a craniopharyngioma was attempted, it was planned to expose the cyst by splitting the optic chiasm and dividing the anterior communicating artery. On March 7, 1940 the right frontal bone flap was reelevated and the tumor exposed. The chiasm and the anterior communicating artery were observed to be stretched across the anterior aspect of a cyst. The artery was divided, and without any additional tension being placed on the optic pathways, the chiasm was cleanly divided in the midline with a scalpel. Thereon the tumor was dissected from the circle of Willis and the partially destroyed hypothalamus. The optic tracts were not adherent to the cyst.

Second Postoperative Course.—The postoperative course was characterized by striking arterial hypotension, tachycardia, peripheral cyanosis and a state of what seemed to be peaceful sleep, which persisted for three days. At no time was there a tendency toward hyperthermia. There was a moderate degree of diabetes insipidus, the specific gravity of the urine ranging from 1.004 to 1.009 and the output between 2,000 and 3,100 cc. per day. By the fourth postoperative day the patient was alert and in fair contact with his surroundings.

Pathologic Report.—The pathologist's report on the tissue removed follows:

"The slides represented cross sections of the lining of a cyst. An epithelial layer was present focally and varied from the stratified squamous to the columnar type. Dipping in from the lining layer and scattered through the deeper tissues were islands of epithelium, chiefly of a basal type and containing small cystic spaces filled with secretion, the staining reactions of which varied from blue to purple or pink.

"The epithelial islands were evidently adamantinomatous foci with enameloblastic activity. They were so widely scattered through the excised tissue that it seemed likely that not all of the growth had been excised. The bulk of the tissue consisted of gliotic brain tissue.

"The diagnosis was that of cyst of Rathke's pouch (adamantinoma)."

Further Course.—There was progressive improvement in every respect until the early part of August 1940. At that time the legs and feet became moderately swollen, and the patient complained of recurrent cramplike pains in the lower extremities. He was readmitted to the hospital for study on Sept. 9, 1940. The visual fields at this time showed classic bitemporal

hemianopsia. The fluid intake and urinary output had decreased. The studies did not disclose the genesis of the edema. This slowly subsided, however, and he returned to school.

Progress was satisfactory until the fall of 1941, when, again, inattentiveness, drowsiness and eventually stupor appeared. The terminal picture was, without doubt, the result of a recurrent growth. Death occurred on Nov. 19, 1941. Permission for postmortem study was not obtained.

It was eleven months after section of the chiasm in the midline that the abnormalities referable to the visual apparatus were studied in detail.

STUDY OF OPHTHALMIC ALTERATIONS

From a review of the neurosurgical picture in this case, it is evident that the ophthalmologic interest depends basically on the midline section of the optic chiasm. A most important consequence of the operative procedure was the visual defect. Studies of the ophthalmic evidence, with special emphasis on the defects in the visual fields, were indicated.

From the evidence recorded in the statement of the surgical problem, it seemed reasonably well established that there was no noticeable reduction of visual acuity and no material defect of the visual field prior to the second phase of surgical intervention. On the occasion of the second operation, every effort was made to avoid unnecessary trauma to the chiasm. The incision which divided that structure in the midline was accomplished with precision. On recovery, the visual field showed classic bitemporal hemianopsia.

It seemed reasonable to assume that the progress of the tumor had of itself not accounted for the field defect, but it was equally obvious that the operative procedure and the healing process might have modified the appearance of the visual field and the degree of visual acuity.

It remained, then, to study the visual fields in detail in order to establish their precise characteristics.[4]

Significant Ophthalmologic Observations.—Other than the aforementioned features, no significant points were disclosed by the general or the ophthalmologic history. The patient had never worn glasses, had had no previous ophthalmologic examination and gave no history of ocular injury or disease. Visual acuity in the right eye at the time the first detailed studies of the visual fields were made (July 10, 1941) was 6/21 (0.3) without correction; in the left eye it was 6/12 (0.5) without correction and 6/12 + 3 (0.5 + 3) with a correction of + 1.50 D. sph., axis 180. There was mild convergence insufficiency; no significant anomaly of accommodation or of pupillary response was noted. Study of the fundus in the usual light showed nothing significant except the uniform primary atrophy of the optic nerve. With a red-free light (Friedenwald ophthalmoscope and a yellow-green filter) the nasal portion of the retina of each eye had a woolly appearance. The temporal portion of the retina gave the characteristic reflex of the nerve fiber layer. No peculiarity of the macula or the paramacular region was disclosed, nor were any changes in the nerve heads apparent with "restricted light." Neither slit lamp

4. It is necessary that we emphasize our attitude toward "relative defects." A relative defect is plotted in response to the subject's description of qualitative variations in the brightness of the (stimulating) object. Hence the scotoma can be no more than a qualitative indication, which may be quite different in size and shape at a subsequent examination, owing to the patient's selection of different descriptive language and standards of brightness. Any reliable defect can be, with appropriate technic, converted into an absolute defect. Under these conditions, the subject merely reports on the presence or absence of the stimulus. The plotted scotoma is measurable, and the conditions of study are reproducible and are less subject to the psychologic whims of the patient. One of us has emphasized elsewhere the clinical unreliability of color fields.[7]

nor other standard methods of study elicited significant evidence. No studies were made of light sense, color sense or perception of movements in the visual fields.

Visual Fields.—As seen in figure 1 *A* and *B*, the field as plotted by means of the perimeter seemed to indicate that the macula had been spared by about 10 degrees. The perimeter, however, is not adapted to precise study of the central fields although projection perimetry was used in this instance, as described elsewhere.[5] Hence a second study (fig. 1 *C*) was made of the fixation region by use of the stereocampimeter and an object 0.4 mm. in diameter.[6] Tests with this object have been shown to give reliable results when fixation is normal.[7] Even with this technic, fixation was not assumed to be perfect, since the corrected visual acuity was not (20/20) 6/6 (1). This led to the conclusion that a central scotoma must be present; so a third study (fig. 1 *D*) was made, the stereocampimeter and a 0.2 mm. object being used. Considerable past experience had shown that

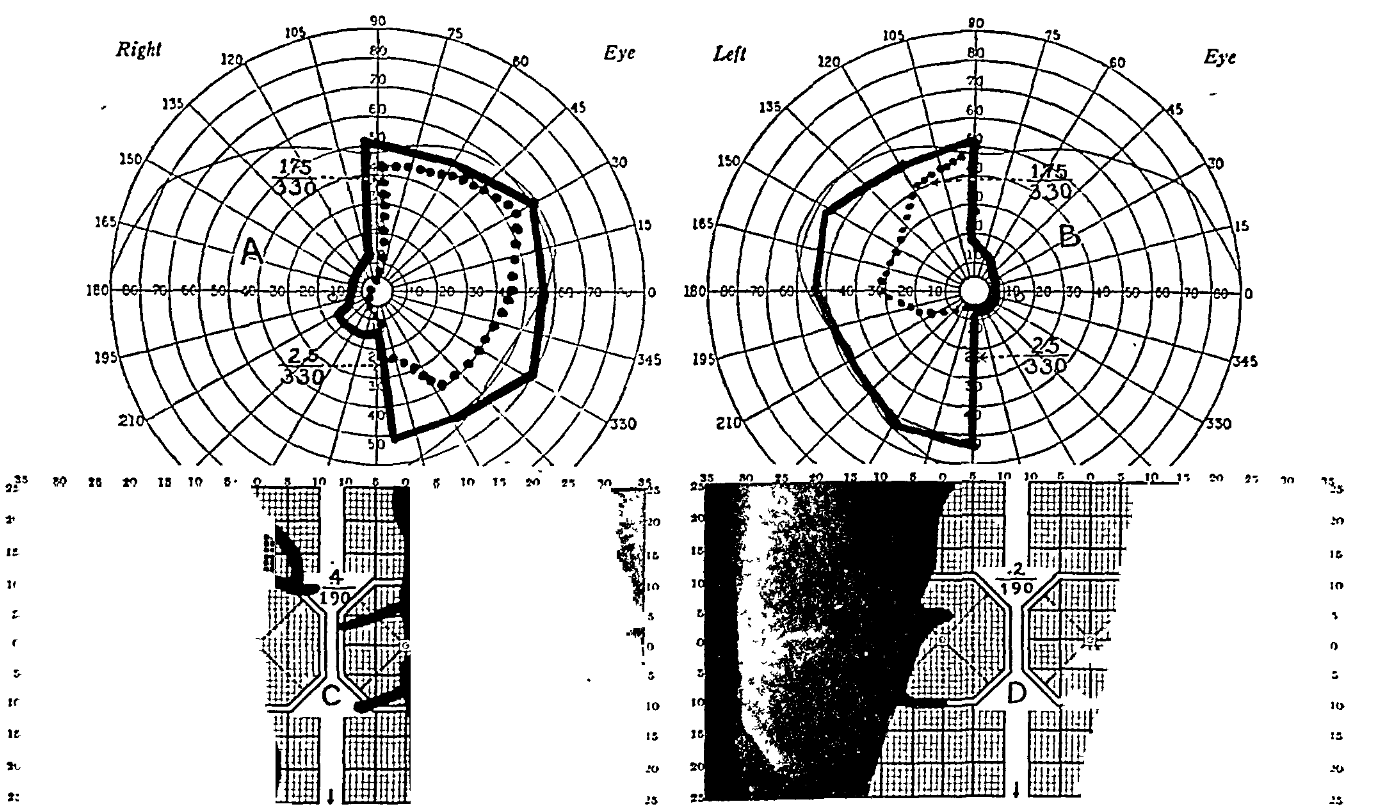

Fig. 1.—Results of surgical anteroposterior division of the chiasm in the case of a 13 year old boy with a craniopharyngioma (tumor of Rathke's pouch). Vision was 6/15 + 3 with correction in the right eye and 6/12 + 3 with correction in the left eye.

A and *B* are perimetric fields, and *C* and *D*, stereocampimetric charts taken with 0.4 and 0.2 mm. objects respectively.

this technic[8] could be depended on to demonstrate a central scotoma even when visual acuity had dropped from (20/20) 6/6 to (20/16) 6/4 so that it seemed likely that it would reliably demonstrate a scotoma capable of reducing 6/6 vision to (20/40) 6/12.

5. Evans, J. N.: The Perimeter Spot-Light Object, Arch. Ophth. **7**:614 (April) 1932.

6. White letters on a black background under 10 foot candles of illumination were used as the test object. These letters were checked for accuracy of size.

7. Evans, J. N.: An Introduction to Clinical Scotometry, Cambridge, Mass., Yale University Press, 1938, pp. 29-43.

8. Though the stereocampimeter was employed, it was used as a monocular device, the affected eye fixing the imaginary center of a drawn circle. A white spherical object was used against a black background at a distance of 190 mm. under 15 foot candles of illumination.

These expectations were fulfilled (fig. 1 *D*) by the demonstration of a finger-like absolute central scotoma which appeared protruding from the blind field above the point fixed. One must realize that the central scotoma could not cover the point fixed, since, macular function being impaired, the paramacular retina was used for this purpose. The true position of the macula was necessarily represented *by some point within the finger-like scotoma.*

From previous studies on a number of patients with strabismus who were subject to central scotoma [9] and from unpublished studies with the ophthalmograph [10] on fixation movements in such subjects and on normal subjects with after-image central scotomas (fig. 2), it was evident that nystagmoid movements must have modified fixation in the present case.[11]

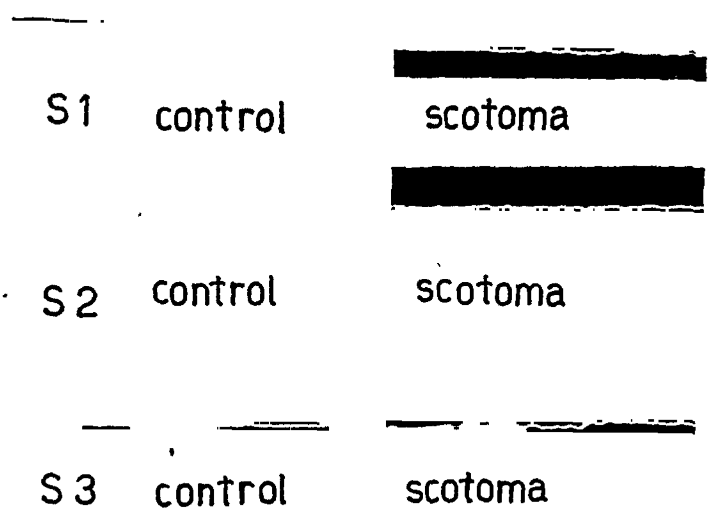

Fig. 2.—Tracing of ocular movements during fixation at 1 meter in a normal subject with after-image central scotoma.

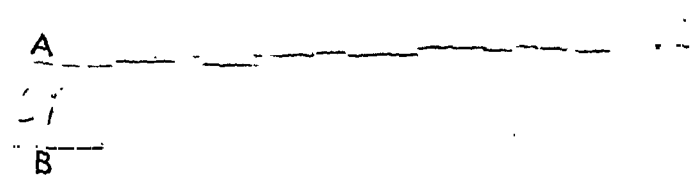

Fig. 3.—Ophthalmographic records of fixation movements. In each instance the subject fixed on a campimeter background (the fixation point being a chalk mark) at 190 mm. through a + 5.25 spherical lens, the conditions of mononuclear fixation as employed during campimetric examination being thus duplicated. A 0.4 mm. object was employed to map in the region of the fixation point.

A indicates the fixation movements of the patient (W. M.), whose chiasm had been divided anteroposteriorly at operation. *B* indicates the fixation movements of a patient who had no known pathologic disturbance of the visual fields or of ocular movements.

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9. Evans, J. N.: Scotoma Associated with Strabismus, Am. J. Ophth. **12**:194 (March) 1929.

10. To all intents and purposes this device is a camera which takes a continuous photograph of the corneal reflex on a moving picture film, which is in continuous motion. The result is a white tracing which represents fixation movements in the horizontal plane.

11. We have long been of the opinion that other workers have not given sufficient consideration to fixation movements when reporting on the shape and size of minute central defects.

In order to comprehend the significance of these movements, the last plotting (fig. 1) was repeated under identical conditions, but with the subject seated before the ophthalmograph. The ophthalmographic reading (fig. 3 *A*), which is presented with a similar tracing for a normal subject (fig. 3 *B*), indicates the expected instability of fixation in the horizontal meridian. It is noted that the so-called normal nystagmoid movements are recorded by the ophthalmograph as an almost unwavering straight line, whereas the tracing for the patient shows many steplike breaks. A great number of these steps were measured from a midline. The average deviation to each side of this midline was 0.89 mm.[12]

It thus seemed evident that these fixation movements modified the size and shape of the scotoma. In order to evaluate this effect, we thought it desirable to determine the actual magnitude of the ophthalmographic variations. To that end a separate study was made, normal subjects being used. The results indicated that the nystagmoid movements covered about 3.75 mm. on the campimetric chart, the horizontal diameter of the scotoma being thereby lengthened by 3.75 mm.

Study of Nystagmoid Movements of Normal Eyes.—With the aid of the ophthalmograph, studies were made on normal eyes to determine the fixation movements that occurred while the subjects were attempting to maintain constant fixation during the plotting of the central visual field. The experiments were so arranged as to duplicate, as nearly as possible, fixation relations as they pertained to clinical studies with the tangent screen and the campimeter at 2 meters, 1 meter, 33 mm. and 190 mm. Repeated attempts to make direct studies in this way demonstrated that the ophthalmograph is not sufficiently sensitive for this purpose. McFarland, Holway and Hurvich [13] apparently arrived at a similar conclusion with regard to the value of the standard ophthalmograph for this purpose.

Another method was therefore employed in order to interpret the deviations of the ophthalmographic record. Experiments on normal subjects were first performed in which fixation was moved successively over five 1 degree jumps and then back to the original fixation point in one 5 degree jump. This was accomplished by having the subject fix. in succession, the center of the 1 degree squares of the stereocampimetric chart. The ophthalmologic record was later projected on a screen for study. By this means it was concluded that a deviation on the ophthalmographic record of 0.71 mm. corresponded to a shift in fixation of 1 degree of the normal eye.

As previously stated (page 48), the fixation movements in the case under study averaged 0.89 mm. on the opthalmographic film during the mapping of the scotoma. It thus seems obvious that the fixation movements in this case covered about 1.25 degrees in the horizontal meridian. Each campimeter square was equivalent to 1 degree and measured 3 mm. in diameter. Thus a deviation of 1.25 degrees in this case was equivalent to 3.75 mm. on the campimeter.

It was recognized that duration of fixation influences the amplitude of oscillations, so that every effort was made to shorten the period during which the patient had to maintain fixation.

Scotometric Studies.—The exact horizontal limits of the scotoma could not be measured because one end merged with the half-field defect.

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12. For convenience, the photographs of these records are placed horizontally in the illustrations; hence horizontal movements of the eyes are shown as vertical steps.

13. McFarland, R. A.; Holway, A. H., and Hurvich, L. M.: Studies of Visual Fatigue, Cambridge, Mass., Harvard University Press, 1942, p. 137.

The length of the scotoma (average values from a number of studies), measured at a level equidistant from the upper and the lower border and extending from its base at the edge of the area of hemianopsia to the tip of the scotoma, was 16 mm. As already stated, the error due to fixation movements would seem to be not greater than 3.75 mm. This is to be subtracted from the plotted length of the scotoma. The horizontal diameter of the scotoma would thus appear to be 12.25 mm. on the tangent surface of the campimeter placed at 190 mm. from the subject's eye (fig. 4).

No graph to show vertical fixation movements was obtained, but such movements must have been minute because the horizontal angioscotoma mapped on each chart as a control of accuracy showed no width greater than one finds in normal subjects. The average width of the angioscotoma of the vessels arching over the macula, determined by measurements of 100 maps carefully selected and controlled to insure reliability, was 4.1 mm., measured on a line bisecting the fixation point (fig. 1 *C* and *D*). Hence it is probable that the horizontal and the vertical diameter of this scotoma were respectively 12.25 and 7.2 mm., or about

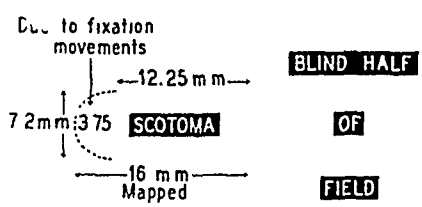

Fig. 4.—Diagram of the scotoma of the macula associated with a defect of the crossed fibers.

4 and 2.5 degrees. This, then, was the size of the scotoma resulting from division of the chiasm in the midline (fig. 4).

It is to be noted that the chart does not show the classic shape of the central scotoma hemianopsia. It is recognized that the shape and size of the scotoma may have been modified by an abnormal angioscotoma, but pressure on the globe did not change the size and shape of this finger-like projection (fig. 1) beyond 9 degrees from its base.[14] In this particular study, the scotoma seemed to have a horizontally oval form. Though some authors have plotted central scotomas which were identical in shape with those associated with hemianopsia, we do not feel that the technic was sufficiently controlled to warrant our acceptance of their results.

If the concept that the macular fibers [15] form a semidecussation in the chiasm is adopted, then in the case cited the surgical procedure divided all the crossed

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14. It has been demonstrated elsewhere [7] that a normal angioscotoma extends horizontally 7 to 8 degrees from the blindspot. This region widened only with pressure on the globe in the present study. The remainder of the defect would thus seem to be due to damage to fiber bundles.

15. For the sake of a clearer mental picture, all consideration of the extramacular fibers of the pathway is omitted.

macular fibers, with the result that the corresponding part of each macula was rendered functionless. This scotoma, then, may be assumed to represent the approximate size and shape of the part of the macula supplied by the crossed fibers (fig. 5).

Since macular function is commonly measured by determination of visual acuity, one is led to inquire what the visual acuity of the intact half-macula should be. A study of this case should supply the answer. Numerous efforts have been made to study the visual acuity of the eccentric retina, but no one, in our opinion, has presented acceptable evidence for various points within the macula. This is because precise fixation cannot be guaranteed.

From evidence supplied by studies reported elsewhere,[7] it seems that a fixing eye with a small central scotoma will be turned or aimed in such a direction as to use the most highly developed isopter which remains undamaged. In this instance (in which it was temporal) the eye would automatically fix with the seeing half-macula (that part of the retina adjacent to the dividing line of the area of hemianopsia). Thus, if in a given case visual acuity (6/6 being accepted as nor-

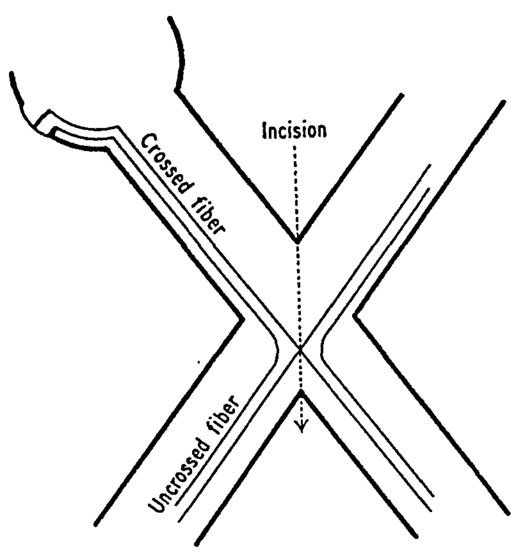

Fig. 5.—Diagram of the macular fibers.

mal) before the damage occurred was 6/6 and remained 6/6 after the hemianopsia had appeared, one might be justified in saying that macular function had been spared. In such a case, the dividing line between the seeing and the nonseeing half-field might show a notable degree of sparing, or it might seem to divide the fixation point. If, on the other hand, vision was reduced to 6/12 and the dividing line seemed to pass directly through the fixation point, one might contend that the macula had been split, with the temporal half left intact and the nasal half[16] destroyed, or one might contend that the entire macular function had been destroyed and that the 6/12 vision represented the retina adjacent to the macula. But we have accepted semidecussation; hence only half the macula can be left. It will be noted that the visual acuity of our subject was about 6/12.

That the dividing line for hemianopsia in this case bends away from the fixation point on the chart (fig. 1), so that the macula is left outside the blind area, is of course not evidence that the macula was spared (fig. 1) unless corrected visual acuity remained normal. It cannot be emphasized too strongly that defective vision not due to a refractive error or to opaque mediums must result

16. The word "half" is used not with the meaning of a mathematically precise portion but in a gross anatomic sense only.

from defect in the visual field in the classic sense. When the visual defect is not explainable by changes in the eyegrounds, it must be referred to damage to visual pathways.

The mere presence of poor vision, then, implies the presence of a scotoma involving fixation, and it must be realized that such a defect cannot coincide with the fixation point as indicated on the plotting chart because that is being fixed by an eccentric portion of the retina not corresponding to the defect. Of course, the subject can displace the central scotomatous area by using the unaffected eye for fixation, but this only obscures the fact that such binocular vision is upset and that the defect is not actually in the plotted position. (The normal eye is fixing with the isopter of 6/6 vision, and the other, with the isopter of 6/12 vision.)

COMMENT

A great many methods have been suggested for maintenance of fixation. The complementary color method of Schlosser, the stereoscopic method of Haitz and the macula selector of Walker were great improvements over earlier ones, but the mere fact that they demand good binocular coordination at a time when one eye is constantly thrown out of line by the scotoma is evidence enough that they cannot secure maintenance of the necessarily refined fixation. Numerous other methods in which the sound eye was supported to steady the eye under study have, of course, been advised. These methods have a justifiable place in the average clinical work, but one gains a false feeling of security because the central scotoma falls so neatly on the fixation point of the chart. A much more perfect check on the accurate positional relation and shape of such a defect is, for instance, the position of the borders of the normal blindspot or of the adjacent angioscotoma. In fact, there is a physiologic effort to line up these mapped normal defects with their tracings on the campimetric chart. The use of these landmarks insures accurate fixation in normal subjects to within 0.25 degree, as concluded from many thousands of studies on angioscotomas; moreover, one can continually check the fixation while plotting the central scotoma. Halstead, Walker and Bucy [17] checked fixation by recording corneoretinal electrical potentials by means of an elaborate, but precise, instrumental setup. This method recorded ocular movements of less than 0.5 degree of arc. (These workers use test objects subtending a visual angle of 15 minutes. It is thus possible that, unknowingly, they may have been plotting angioscotomas—possibly pathologically enlarged or widened by such factors as menstruation and low blood pressure. These same investigators also checked their work, in certain instances, by means of a camera for ocular movements. Their equipment also recorded movements of the head and the subject's responses to disappearance of test objects. They could check both vertical and horizontal ocular movements. Their camera did not seem to be the well known ophthalmograph.)

It thus seems justifiable to assume that the present study, with the technic of angioscotometry, is as accurate and dependable as the more elaborate and less clinically useful methods employed by other workers. One could not conclude, however, that the nystagmoid movements studied arose from the presence of the central scotoma alone, as the surgical traumatism and the pathologic process may have contributed to their production. In fact, it cannot positively be contended that the scotoma was entirely due to the splitting of the chiasm, because other, and

17. Halstead, W.; Walker, A., and Bucy, P.: Sparing and Nonsparing of "Macular" Vision Associated with Occipital Lobectomy in Man, Tr. Sect. Ophth., A. M. A., 1940, p. 193. Their special instrument showed sparing of the macula of 2.5 degrees.

considerable, damage must have occurred from the surgical measures and the action of the tumor and healing process.

Reports of this type are definitely worth while, however, if supported by enough corroborative evidence from studies of a similar type. One other aspect of this subject might receive consideration. In the present case a scotoma due to a lesion of the crossed macular fibers extending into the field of the seeing (temporal) portion of the retina has been noted. If the line between the seeing and the blind half of the retina runs through the fixation point, it is necessary to explain how the blind nasal area of the macula is found in the seeing temporal extramacular field. If the projection of the macula is regarded as a field separate and distinct from the rest of the projected retina, then it can be assumed that the macular field is eccentrically placed in the extramacular field. It is not possible to determine the degree of eccentricity until a study of the field resulting from dysfunction of the uncrossed macular fibers has been made. It seems impossible to make such a study by division of the uncrossed fibers, but perhaps some case may appear in which the field of the intact papillomacular bundle will alone remain undamaged (as in cases of quinine poisoning). It will then be possible to compare the results with the observations in the case here presented and to deduce the character and extent of the defect characteristic of dysfunction of the uncrossed macular fibers. That nasal elements are offset in the temporal area is not a novel idea when it is recalled that the papilla containing temporal fibers is far offset to the nasal side. Reference to figure 5 shows a simple and possible arrangement of fibers which may help to explain this point.

One must also keep in mind possible anatomic variations which might bring the line of crossing of macular fibers to one side of the chiasm, so that final visual acuity would vary from case to case.[18]

It is altogether possible that both crossed and uncrossed macular fibers supply the whole macular area so that the scotoma shown represents only a partially blind, or "depressed," area, a possibility accounting for the offset position of the defect and the reduced visual acuity.

CONCLUSIONS

The results of the present study seem to permit the following conclusions:

The methods we have employed in this study are more adequate than those of other workers.

The visual acuity resulting from division of the crossed macular fibers is approximately (20/40) 6/12 and permits the subject to read and write such material as he is apt to need in average daily lfie.

The divided macular fibers crossing in the optic chiasm in this case did not give rise to the half-moon scotoma.

Fixation movements require consideration in determination of the size and shape of the defect.

The entire macula must be supplied by both crossed and uncrossed fibers.

These observations should be of assistance to the neurosurgeon and the ophthalmologist, who may have occasion to study similar cases.

23 Schermerhorn Street.

200 Hicks Street.

18. In Haden's case vision in the left eye was 6/6. "Electrical" cutting was used to divide the chiasm in this case.

PENICILLIN AND SULFADIAZINE IN THE TREATMENT OF EXPERIMENTAL INTRAOCULAR INFECTIONS WITH STAPHYLOCOCCUS AUREUS AND CLOSTRIDIUM WELCHII

LUDWIG VON SALLMANN, M.D.
NEW YORK

The study of the chemotherapy of intraocular infections of the anterior segment with Diplococcus pneumoniae [1] was extended in these experiments to similar infections with Staphylococcus aureus, which stands second to D. pneumoniae in frequency as the cause of post-traumatic and postoperative purulent endophthalmitis, and Clostridium welchii was selected as a representative of the anaerobe group. The effect of the oral administration of sulfadiazine in combination with the topical use of its sodium salt was again compared with that of the local treatment with penicillin.[2]

INFECTIONS WITH STAPHYLOCOCCUS AUREUS

Preliminary Experiments.—Eight strains of Staph. aureus, obtained in cultures of material from human conjunctivas and corneas,[3] were tested in vitro for their sensitivity to penicillin. The determinations were made in accordance with the modified method of Fleming [4] except for the use of a 10^{-2} dilution of the broth culture in place of a loopful of the latter per 5 cc. of broth. Two strains of mannitol-positive hemolytic Staph. aureus of average sensitivity to penicillin were used for inoculation of the eyes of mature chinchilla rabbits. Strain W was isolated from the conjunctiva of a patient with severe postoperative endophthalmitis. Strain K was grown from material obtained from a fulminant corneal ulcer of a diabetic patient. The injection of cultures of these strains into the anterior chamber did not lead with certainty to severe destructive endophthalmitis. Such an inflammation was produced, however, when the surface of the lens was deeply incised during the procedure of inoculation. The standard lesion thus obtained was a satisfactory test object for the chemotherapeutic experiments with staphylococci. The histologic changes were studied at various stages of the infection.

TECHNIC

Inoculation.—The pupils were dilated with atropine; moderately deep sleep was induced with pentobarbital sodium, and local anesthesia was effected with a 0.1 per cent solution of *nupercaine hydrochloride*. The technic described in the experiments with pneumococci was modified to avoid the injection of air after the withdrawal of aqueous and the insertion of the syringe filled with the diluted culture. A small three way stopcock was armed with a 27 gage needle and connected with two tuberculin syringes. The needle was introduced into the anterior chamber near the limbus at 12 o'clock, and a large, deep slit was made in the anterior cortex of the lens. Aqueous was withdrawn into one syringe, and after the proper adjustment of the stopcock, a net amount of 0.05 cc. of a 10^{-4} dilution of an eighteen hour broth culture was injected into the anterior chamber. The number of viable organisms injected, as calculated by plate counts, varied from 5,000 to 10,000. After

This study was supported by the Knapp Memorial Foundation.

From the Department of Ophthalmology of Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology, Presbyterian Hospital.

1. von Sallmann, L.: Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with Pneumococcus, Arch. Ophth. **30**:426 (Oct.) 1943.

2. The penicillin was extracted and prepared in the laboratory of Dr. Karl Meyer.

3. Dr. Devorah Locatcher-Khorazo did all the bacteriologic work on the human eye in connection with this experimental study.

4. Fleming, A.: In-Vitro Tests of Penicillin Potency, Lancet **1**:732, 1942.

withdrawal of the needle an attempt was made to seal the puncture canal with a heated probe, but in many instances some fluid leaked out of the wound. The lids were kept closed for several hours by fixing the upper lashes on the cheek with a small strip of cellulose tape.

Treatment.—Treatment was initiated six to seven hours after inoculation and consisted of the iontophoretic introduction of sulfadiazine or of penicillin. The ionization method was selected for local therapy because previous experiments [5] had shown that it greatly increased the concentration of both drugs in the aqueous. In addition, this treatment had been found to be well tolerated by the human eye. Application of sodium sulfadiazine in a 5 per cent solution for five minutes at 2 milliamperes was supplemented by the oral administration of 0.25 Gm. of sulfadiazine per kilogram of body weight each day. Sodium penicillin was used locally in a solution of 0.25 per cent at the same millamperage and for the same length of time as the sulfonamide salt.[6] The local applications were generally repeated twice a day on the two succeeding days (one application of five minutes and one of three minutes) and once a day for the next three days. Treatment was discontinued if the anterior segment became completely suppurative.

RESULTS OF PRELIMINARY EXPERIMENTS

Of the 8 manitol-positive strains of hemolytic Staph. aureus, 5 were isolated from the conjunctiva, 2 from corneal ulcers and 1 from a cystoid scar resulting from an Elliott trephination followed by a severe late infection. Four of the strains were obtained from patients whose eyes had been treated unsuccessfully with sulfonamide drugs for several months in preparation for extraction of cataract. The sensitivity to penicillin of all strains was within the same range; that is, growth in a 10^{-2} broth culture was inhibited by 0.187 to 0.625 microgram per cubic centimeter of a relatively crude preparation of penicillin. The strain with the greatest sensitivity to penicillin (0.187 microgram per cubic centimeter) showed less virulence than other strains on inoculation into the anterior chamber of rabbits.

The conjunctiva and the border of the lid of 2 patients were rendered free of sulfonamide-fast strains of Staph. aureus haemolyticus two and five days respectively after treatment consisting of hourly instillations of a 0.25 per cent solution of sodium penicillin for a daily period of twelve hours. For 2 additional patients the cultures were negative twenty-four hours after initiation of the treatment, but no previous attempt had been made to influence the flora with sulfonamide compounds.

The clinical and histologic inflammatory changes observed six hours after inoculation of the eyes of rabbits were caused in great part by the trauma of the injection. To this category belong the dense fibrinous exudate in front of the pupil, the dilatation of the capillaries in the iris and the ciliary body, the obvious increase in protein content of the aqueous, the presence of a few polymorphonuclear leukocytes in the iris and the anterior chamber and the characteristic edema of the ciliary processes in the form of numerous Greeff blebs. The changes agree well with the signs of inflammation described by Poos [7] as the hypotonic effect of paracentesis in rabbits. The presence of clumps of polymorphonuclear leukocytes in the anterior chamber and the purulent exudate at the pupillary border should be attributed to the infection since these signs were not evident in control eyes with

5. (*a*) von Sallmann, L.: Sulfadiazine Iontophoresis in Pyocyaneus Infection of Rabbit Cornea, Am. J. Ophth. **25**:1292, 1942. (*b*) von Sallmann, L., and Meyer, K.: Penetration of Penicillin into the Eye, Arch. Ophth., this issue, p. 1.

6. A calcium salt of penicillin was prepared by Dr. Karl Meyer for tentative experiments with iontophoresis in a series of 8 eyes. The iontophoretic introduction of a 0.25 per cent solution caused an extensive abrasion of the cornea and fibrinous exudate in the anterior chamber.

7. Poos, F.: Ueber die histologischen und klinischen Erscheinungen bei akuten, lokalen Capillarkreislaufstörungen am Auge, Arch. f. Ophth. **127**:489, 1931.

injections of sterile broth. In many instances the clumps of leukocytes, suspended in the fibrin network in front of the cataractous lens, could be seen macroscopically

At this stage sections stained by Verhoeff's [8] modification of the Gram-Weigert method revealed numerous organisms on the surface of the exposed lens fibers. No organisms could be detected with certainty in other parts of the anterior chamber. Beginning invasion of the wound in the lens by polymorphonuclear leukocytes was noted.

All signs of inflammation increased greatly in the following eighteen hours. This stage was characterized by a dense infiltration of the limbus and extensive purulent exudate in the anterior chamber, with several layers of leukocytes at the posterior surface of the cornea. The deeper staining of the anterior and the posterior chamber with eosin indicated the high protein content, but frequently only a few leukocytes were present in the posterior chamber and vitreous cavity. The wound in the lens was covered with exudate and masses of leukocytes, which also infiltrated the superficial and the deeper layers of the anterior cortex.

Results of Sulfadiazine and Penicillin Treatment Beginning Six to Seven Hours After Injection of a 10^{-4} Dilution of Staph. Aureus into the Anterior Chamber with Simultaneous Injury of the Lens

Treatment	Strain of Staph Aureus Injected	Number of Eyes	Number of Eyes: Recovered	Temporarily Improved	Lost
Sodium sulfadiazine iontophoresis and oral use of sulfadiazine	W	11	4	—	7
	K	12	1	—	11
Control eyes (influenced only by oral use of sulfadiazine	W	5	1	—	4
	K	8	—	—	8
Sodium penicillin iontophoresis	W	12	6	3	3
	K	12	9	—	3
Control eyes (no treatment)	W	10	—	—	10
	K	9	—	—	9

In the later stages the purulent endophthalmitis spread into the posterior chamber and the vitreous, soon involved the nerve head, destroyed the retina and finally the choroid and so led to the histologic picture of panophthalmitis.

RESULTS OF TREATMENT

The course of the experimental endophthalmitis and the results of the treatment indicated that strain K had a higher animal pathogenicity than strain W and that infections with the first strain were more difficult to control by either type of chemotherapy (table).

Five out of 23 eyes were saved by the combined oral and topical use of sulfadiazine. The other 18 eyes were destroyed by the infection. The condition in 1 of 12 eyes infected with strain K was cured by therapy with the sulfonamide compound

Fifteen out of 24 eyes were successfully treated by the local use of sodium penicillin. In 6 eyes the inflammation progressed from the beginning in spite of

8. Verhoeff, F. H Observations on Parinaud's Conjunctivitis (Leptothricosis Conjunctivae), Am. J. Ophth 1:706, 1918

the therapy. The other 3 eyes were considered healed after treatment for three days, but the inflammation flared up about a week later. It could not be checked by renewed treatment with penicillin. The therapy was continued a few days longer in the succeeding series, and thereafter no relapses occurred. Nine out of 12 eyes infected with strain K responded well. In 1 rabbit one eye was treated with sodium penicillin and the other with sodium sulfadiazine; in addition sulfadiazine was given orally in the usual dose. The eye treated locally with the sulfonamide compound suppurated; the infection in the penicillin-treated eye was checked.

In all 19 untreated control eyes of the penicillin series destructive purulent endophthalmitis developed. The infection cleared up in 1 of the 13 control eyes of the sulfadiazine series which were influenced by the daily oral administration of 0.25 Gm. of sulfadiazine per kilogram of body weight.

Penicillin therapy produced three times the number of good results as did the combined sulfadiazine treatment (62.5 to 21.7 per cent). This contrast would presumably have been even more striking (75 to 21.7 per cent) if the period of treatment with penicillin had been extended a few days longer in the first group of experiments.

COMMENT

Thygeson,[9] in his review of the treatment of ocular infections with sulfonamide compounds, stated that staphylococci are relatively resistant to these substances. He found, however, that topical applications were of value for external infections with this organism, such as blepharitis, conjunctivitis and corneal ulcer. He also reported 7 cases of intraocular infection with staphylococci, in 4 of which the condition responded satisfactorily to treatment with a sulfonamide compound, in 2 slowly and in 1 not at all. In 5 of 7 cases of staphylococcic panophthalmitis previously listed by Guyton and Woods [10] treatment with sulfonamide compounds was successful. In the absence of operation, the certainty of the etiologic diagnosis in cases of endophthalmitis and panophthalmitis not of metastatic origin is weakened, however, by the recognized difficulties of the bacteriologic examination.

The experimental work on modern chemotherapy of staphylococcic infections of the eye has been confined to corneal inoculations. No conclusions can be drawn from the single observations of Meoni,[11] but the extensive study of Robson and Scott [12] is informative in its comparison of the effects of various chemotherapeutic agents on a fairly well standardized corneal lesion. Penicillin was found more beneficial than sulfacetimide, and also more effective in prevention. The use of "solubilized" sulfathiazole [13] gave disappointing results, and tyrothricin [14] was of only slight benefit. To my knowledge no experimental data on the results of chemotherapy of intraocular infections with staphylococci are on record.

The reliability of the standardized intraocular lesion reported in the present paper is open to criticism. To the general inaccuracies of biologic experiments must be added the following possibilities of error inherent in the technic: The unavoidable escape of an uncontrolled amount of the injected broth culture resulted

9. Thygeson, P.: Sulfonamide Compounds in Treatment of Ocular Infections, Arch. Ophth. **29**:1000 (June) 1943.

10. Guyton, J. S., and Woods, A. C.: Use of Sulfanilamide in Ophthalmology, Am. J. Ophth. **24**:428, 1941.

11. Meoni, M.: La chemioterapia sulfamidica nelle affezioni oculari, Arch. di ottal. **46**: 183, 1939.

12. Robson, J. M., and Scott, G. I.: Local Chemotherapy in Experimental Lesions of the Eye Produced by Staphylococcus Aureus, Lancet **1**:100, 1943.

13. "Solubilized" Sulfathiazole is a 15 per cent solution of sulfathiazole sodium formaldehyde sulfoxylate.[12]

14. Tyrothricin consists of 15 per cent gramicidin and 85 per cent tyrocidin.

in variations in the size of the inoculum. The depth and extent of the opening in the lens and the intensity of the trauma were also not constant. The course of the control lesion was sometimes fulminant and sometimes subacute. To compensate for the differences in the initial lesions, however, the eyes with more pronounced inflammatory reactions as observed, with the slit lamp were selected for local treatment, and those with minor signs of infection were used as controls.

The contrast between the efficacy of sulfadiazine and that of penicillin noted in treatment of experimental intraocular infections with pneumococci was not as striking in experiments with staphylococci. It was evident, however, that the topical application of penicillin definitely checked infections with two strains of Staph. aureus much more frequently than did combined sulfadiazine therapy. The results in the sulfadiazine series illustrate, again, the importance of supplementation of systemic therapy with local treatment. The topical application of penicillin shows the effect of comparatively high levels in the aqueous exerted for several hours. It is probable that the number of good results can be increased by combining iontophoresis with a method which will produce a moderate but sustained level of penicillin in the aqueous. Previous attempts to obtain this condition by the repeated use of ointments or instillations, including the combination with wetting agents, did not result in any noticeable antibacterial activity of the aqueous.[5b] No attempts were made to introduce penicillin systemically, for reasons cited in the same paper.

Florey and Florey [15] emphasized that a bacteriostatic concentration of penicillin must be maintained at every point at which there are infecting organisms. Desirable as this aim may be, it is difficult to attain in the various structures of the eye. A continuous bacteriostatic concentration may be obtained in the aqueous with improved therapeutic methods, but in the lens or vitreous it can hardly be achieved without an extreme and sustained rise of the level of the drug in the aqueous or the blood. It is of interest, therefore, that a large number of infections of the lens were checked by a method which produced only a transient high concentration of the antibiotic agent in the aqueous. The high levels obtained by iontophoresis are not essential, however, in treatment of infections of the anterior chamber without injury to the lens, as the use of the corneal bath in cases of pneumococcic infection showed.[1] In general it may be assumed that with acute, virulent infections with organisms of moderate sensitivity to penicillin, especially those involving the lens, higher concentrations are desirable.

The humoral and cellular body defenses, although unable to overcome the experimental infection of the lens, are certainly of importance in the final outcome. In view of the results, there is no reason to assume that iontophoresis interferes with body defenses, or if such interference does occur, it is compensated for by the beneficial effect of the chemotherapeutic compounds. Further studies are necessary to clarify various aspects of this problem.

The question of corneal damage by the treatment was discussed in a previous paper.[1] Since then iontophoretic applications with penicillin have been used in a series of patients, and no undue effects, especially no abrasions, have been noted.[16] In rabbits, abrasions occurring after repeated applications on the same

15. Florey, M. E., and Florey, H. W.: General and Local Administration of Penicillin, Lancet **1**:387, 1943.

16. An applicator tube, similar to that of van Heuven, and made of lucite by Obrig Laboratories, New York, was found useful for clinical purposes. One end of the tube has a broad flare, in the form of the scleral part of a contact lens. The diameter of the opening is approximately that of the cornea. Five millimeters above this aperture a spiral of platinum wire is contained in a widening of the tube. An extension of the wire provides a connection to the lead of the apparatus for iontophoresis.

day generally heal quickly, but in 2 animals (1 in the pneumococcus series and 1 in the staphylococcus series) a large abrasion was followed by a strong inflammatory reaction, leading to a central scar. These experimental results are in agreement with Bellows'[17] observation that "topical application of [sulfonamide compounds] to the denuded cornea retards epithelial regeneration and promotes scarring." Corneal lesions can be avoided, however, even in the more sensitive cornea of the rabbit, by proper timing of the treatment and adequate dosage.

The importance of continuation of penicillin therapy for a few days after the inflammation appears to be checked macroscopically was mentioned in experiments with pneumococci. Florey and Florey[15] also stressed the indication for continued treatment after an apparent cure. These statements were confirmed by the occurrence of relapses in 3 cases of staphylococcic infection in which iontophoretic applications were discontinued too soon.

In experimental infections of the cornea with staphylococci the value of sulfonamide compounds and of penicillin lies, according to Robson and Scott,[12] in the prevention of acute infections rather than in their treatment, as these authors obtained good results only when chemotherapy was begun one hour after inoculation. Observations on intraocular infections treated with penicillin do not support their opinion. Penicillin was effective in many eyes with an initially violent inflammation. This was especially noticeable in the gradual improvement of pneumococcic infections with a twelve hour interval between inoculation and treatment. The definite therapeutic activity of penicillin was further indicated by its control of 3 cases of progressive pneumococcic endophthalmitis resistant to sulfadiazine therapy.[1] No beneficial effect was evident in eyes in which the acute endophthalmitis had reached a climax. The six hour interval between the infection and the first treatment was not extended in experiments with injury to the lens because the more violent infections pursued an acute course and reached a climax within twelve hours.

The experimental results of treatment with sulfadiazine and penicillin were obtained on infections with two strains of staphylococci. The eight strains tested in vitro varied slightly in their susceptibility to penicillin. Nevertheless, no general conclusions should be drawn in regard to the effectiveness of the treatment, since Hobby and her co-workers[18] and Fleming[4] have found strains of staphylococci with a very low sensitivity to penicillin. The frequency of the occurrence of insensitive strains in the eye cannot be judged in view of the small series examined.

The experimental results can be applied to human postoperative and post-traumatic purulent endophthalmitis only with great reservation. A few essential differences between the human infection and the experimental lesion must be emphasized. The size of the inoculum would be much smaller in the case of the human infection, but the interval between infection and treatment would probably be longer. In addition, there may exist primary involvement of deeper layers of the lens and of the posterior segment of the eyeball. The condition in infected human eyes is difficult to reproduce in animal eyes because of the higher incidence of spontaneous recovery in the latter. The results reported here are concerned with acute intraocular infections caused by a large inoculum. For this condition local application of penicillin is more effective than the combined sulfadiazine

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17. Bellows, J. G.: Chemotherapy in Ophthalmology, Arch. Ophth. **29**:888 (June) 1943.
18. Hobby, G. L.; Meyer, K., and Chaffee, E.: Activity of Penicillin in Vitro, Proc. Soc. Exper. Biol. & Med. **50**:277, 1942.

therapy, although the latter may be of great practical value in treatment of milder staphylococcic infections of the human eye.

II. INFECTIONS WITH CL. WELCHII

The frequency of post-traumatic and postoperative intraocular infections with anaerobes is not known. Although only 27 cases have been reported in the literature, it is generally assumed that their occurrence is less rare than the number of published cases would indicate. Morax[19] saw 1 case of ocular infection with Cl. welchii following explosion of a grenade in World War I; he explained the scarcity of cases by the technical difficulties of the bacteriologic examination. A better judgment of the relative frequency of anaerobic infections of the human eye may be attained on the basis of their clinical diagnosis, as described by Ridley[20] and Hamilton[21] and especially stressed by Rieger.[22] It is believed that panophthalmitis generally follows an anaerobic infection of the eye.

Infections were produced in the eyes of rabbits by Chaillous[23] and Schumacher[24] and in extensive, systematic studies by Morax and Chiazzaro.[25] Schumacher produced suppuration of the anterior segment by the injection of an undiluted broth culture of Cl. welchii into the anterior chamber. The other authors did not produce any change or obtain more than transitory iritis with this technic. Morax and Chiazzaro, however, succeeded in producing almost regularly a severe endophthalmitis ending in panophthalmitis by injection of spores of various species of anaerobes into the lens. The observations reported in this paper confirm the results of Chaillous and of Morax and Chiazzaro.

PRELIMINARY EXPERIMENTS

The injection of Cl. welchii (0.05 cc. of a 10^{-1} dilution of an eighteen hour culture in thioglycollate broth) into the anterior chamber did not produce progressive endophthalmitis suitable as a test object. The technic applied successfully in experiments with pneumococci and staphylococci, that is, injury of the lens at the time of injection, also did not establish anything more than a self-limiting iritis of short duration. The intralenticular injection of Cl. welchii (0.05 cc of a 10^{-4} dilution in isotonic solution of sodium chloride) regularly produced purulent endophthalmitis of a subacute or chronic course, which was followed by complete destruction of the inner layers of the posterior segment of the eye. This method was a modification in minor points of that described by Morax and Chiazzaro.

The pupil was dilated with atropine and the eye anesthetized with a 0.1 per cent solution of nupercaine hydrochloride. A 27 gage needle was used to perforate the cornea at the limbus at 12 o'clock and was inserted obliquely in the

19. Morax, V.: Des infections du globe oculaire par microorganismes anaérobies, Bull Acad. roy. de méd. de Belgique **7**:321, 1927.

20. Ridley, F.: Gas Gangrene Panophthalmitis, Tr. Ophth. Soc. U. Kingdom **49**:221, 1929.

21. Hamilton, J. B.: Notes on B. Welchii Infection of the Globe, Brit. J. Ophth. **14**:452, 1930.

22. Rieger, H.: Ueber Wundinfektion des Augapfels mit Erregern der Gasbrandgruppe, Arch. f. Ophth. **137**:61, 1937.

23. Chaillous, J.: Deux cas d'infection traumatique du globe oculaire par un microbe anaérobie (Bacillus perfringens), Ann. d'ocul. **134**:115, 1905.

24. Schumacher, G.: Anaërobe Bazillen bei Augenverletzungen, Klin. Monatsbl. f. Augenh. **46**:34, 1908.

25. Morax, V., and Chiazzaro: Sur l'infection du cristallin: Recherches cliniques et expérimentales, Ann. d'ocul. **164**:241, 1927.

anterior cortex of the lens in the pupillary area. The fluid was then injected into the region of the anterior pole.

The technic of treatment was the same as that in experiments with staphylococcic infections.

Preliminary experiments consisted of the in vitro determination of the sensitivity to penicillin of two strains of Cl. welchii and of the study of the course of the untreated infection after intralenticular injection of the dilution of the culture. Both strains were found to be relatively insensitive to penicillin, as 6.25 to 12.5 micrograms per cubic centimeter of a rather crude preparation of penicillin was necessary to inhibit the growth of a 10^{-1} dilution of an eighteen hour culture in thioglycollate broth with the serial dilution method of Fleming.[4]

The various stages of the infection were studied clinically and histologically in 20 control eyes, which were enucleated two to thirty-eight days after injection. The inflammatory signs attributable to the infection developed usually within forty-eight hours. At that time a moderate amount of purulent and fibrinous exudate was seen in the anterior chamber. Infiltrations of various extent were visible in the lens, and circumscribed patches of purulent exudate were noted on its posterior surface. During the first week the infection was generally confined to the cornea, lens, iris and ciliary body. After this the acute inflammation extended in most instances into the vitreous space, the optic nerve and the retina. As a rule the surface of the optic disk was the first area of the eyeground on which leukocytes accumulated. Detachment of vitreous was seen in the early and in the late stage of the infection. The signs of inflammation in the anterior segment often regressed after the third or fourth week. The injection of the eyeball disappeared; the anterior chamber became clear, and the contracted pupil was closed by an occlusion membrane. Dissection and histologic examination of the eye at this period disclosed an abscess of the vitreous, advanced disintegation of the lens and complete detachment of the retina. In a few instances the choroid was densely infiltrated before the retina was destroyed. The inflammation remained localized in the eye, and no signs of a systemic infection were noted during the period of observation.

Gram stains were made of all eyes. Verhoeff's method[8] gave better results than the Gram-Weigert technic and revealed the presence of a moderate or large number of morphologically characteristic gram-positive bacilli lying within the substance of the lens of all eyes. In many instances the capsule of the lens had been digested away, and infiltrated, necrotic lens material protruded into the anterior and posterior chambers or into the vitreous space. Apparently, the distribution of the bacilli depended in part on the pressure of injection and on the site of the needle tip during injection. In the early stage of the infection, however, foci of bacilli were seen in the anterior layers of the lens or in deeper parts of the anterior half. In later stages the foci were observed near the posterior surface or beneath the posterior capsule of the lens. The substance of the lens had lost its fibrillar structure in the areas of bacillary foci. Bacilli were frequently seen in great numbers at the border of the infiltration but rarely within the infiltrated area. They were not seen outside the lens or apart from the lens substance, and their number did not decrease noticeably in the later stages of the endophthalmitis.

RESULTS OF TREATMENT

Combined sulfadiazine therapy was used in 4 eyes and local penicillin therapy in 8 eyes. The second eye of each of the 12 rabbits was kept as a control. The clinical appearance of the eyes treated with the sulfonamide compound suggested a

beneficial effect in 1 eye and no effect in 3 eyes. The inflammatory process in 1 of the treated eyes advanced more rapidly than that in the control eye. No influence of the systemic treatment was evident on comparison of the control eyes of rabbits which received sulfadiazine orally with the control eyes of the animals not so treated. Three eyes of the penicillin series presented fewer signs of inflammation than their controls. The treated and untreated eyes of 3 other rabbits showed no differences, and in 2 rabbits the endophthalmitis appeared to have progressed further in the treated eyes than in the control eyes. The impression of a favorable effect of the treatment in 1 out of 4 rabbits in the sulfadiazine series and in 3 out of 8 rabbits in the penicillin series was not substantiated by the histologic examination of the posterior segments of the treated eyes. The infection had progressed behind the lens-iris diaphragm with the same intensity as in the control eyes despite the improvement of the endophthalmitis in the anterior segment.

At an early stage of the infection one eye of a rabbit in the penicillin series showed strikingly less infiltration and purulent exudate than the control eye after two days of treatment. On histologic examination the lens of this eye, as well as the lenses of all treated eyes, was found to have a large number of well stained, morphologically normal bacilli. It can be assumed, therefore, that the course of the infection was only delayed in this eye. No beneficial effect of the therapy was noticed in regard to the number or distribution of the bacilli and the extent of the infiltration in the lens.

COMMENT

The technic which was successful in establishment of a standard lesion with D. pneumoniae and Staph. aureus failed to produce a reliable test object of the anterior segment of the rabbit eye with Cl. welchii. Deleterious endophthalmitis was obtained only on injection of a dilution of the broth culture directly into the lens. The results of chemotherapy in experiments with Cl. welchii cannot be compared with those in the experiments with pneumococci and staphylococci because of the much more favorable experimental conditions in the latter.

Traces up to 1.3 mg. of the sulfadiazine drug per hundred grams of infiltrated lens were observed in 4 eyes after combined sulfadiazine therapy (one hour after iontophoresis and three hours after the oral administration of 0.25 Gm. per kilogram of body weight). Bellows and Chinn [26] reported 1.1 mg. of sulfapyridine per hundred grams of tissue and no sulfathiazole in the intact lens four hours after oral administration of the compounds. P'an [27] found 2.4 mg. of the sulfonamide drug per hundred grams of the lens after the local use of sulfapyridine but none after the application of sulfathiazole and sulfadiazine powder. It is reasonable to assume that penicillin enters the inflamed lens in the same moderate proportion as do the sulfonamide compounds. The experimental conditions for the effective treatment of infection with Cl. welchii were further impaired by the comparatively low sensitivity of the two strains to penicillin.

From the results of these experiments it appears unlikely that the treatment of anaerobic infections of the human eye involving deeper layers of the lens can overcome the twin disadvantages of the low susceptibility of the organisms to penicillin and the poor permeability of the lens.

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26. Bellows, J. G., and Chinn, H.: Penetration of Sulfathiazole in the Eye, Arch. Ophth. **25**:294 (Feb.) 1941.

27. P'an, S. Y.: Ocular Absorption of Sulfonamide Derivatives After Local Application, Proc. Soc. Exper. Biol. & Med. **49**:384, 1942.

SUMMARY

1. Injections of various strains of Staph. aureus into the anterior chamber of the eyes of chinchilla rabbits with simultaneous injury of the lens produced a reliable standard lesion for chemotherapeutic experiments.

2. Combined oral and topical use of sulfadiazine was beneficial in 21.7 per cent of the eyes with purulent endophthalmitis produced by the aforementioned means when treatment was initiated six to seven hours after inoculation.

3. Penicillin, applied topically with the first treatment six to seven hours after inoculation, controlled the infection definitely in 62.5 per cent and possibly in 75 per cent of the eyes.

4. Intralenticular injections with Cl. welchii caused destructive endophthalmitis.

5. Neither sulfadiazine nor penicillin therapy begun six hours after the intralenticular injection of Cl. welchii had any effect on the resulting endophthalmitis.

Miss J. Di Grandi and Miss C. Zink assisted in this study.

Columbia University College of Physicians and Surgeons.

KERATITIS OCCURRING WITH MOLLUSCUM CONTAGIOSUM

OTIS S. LEE Jr., M.D.
IOWA CITY

Molluscum contagiosum is an infectious disease of the skin characterized by the formation of multiple, small, discrete, umbilicated epithelial nodules. These nodules, appearing most commonly on the face and hands of young persons, are usually circular, average 2 mm. in diameter and are covered with normal epithelium. In the center of the characteristic umbilication is an orifice from which a cheesy mass consisting of ovoid cells, termed molluscum bodies, can be expressed. Microscopically these bodies are composed of swollen and vacuolated epithelial cells having an atrophic nucleus which has been pushed to one side by an acidophilic cytoplasmic inclusion body. These inclusions are composed of minute elementary bodies, first described by Lipschütz,[1] and are thought by some investigators to be the causative virus. The virus origin of molluscum contagiosum was established in 1905 by Juliusberg,[2] who demonstrated that the disease was transmissible from person to person by material which had passed through Chamberland filters.

Although molluscum contagiosum has been described as a relatively common cutaneous condition, it rarely appears on the eyelids; however, Elschnig[3] observed an incidence of 1 in 2,500 cases in the Eye Clinic at Prague, and Quill,[4] at the Mayo Clinic, reported that it affected the lids in 11 of 128 cases of the disease. In the clinic of this university only 3 cases have been encountered in the past fifteen years.

The appearance of molluscum contagiosum on the eyelids is similar to that elsewhere on the skin. Clinically, it must be distinguished from nevus, fibroma, verruca and epithelioma. The diagnosis is confirmed by microscopic examination of the excised lesions.

Molluscum contagiosum nodules along the margins of the lids may produce follicular conjunctivitis, an association first recognized by de Wecker[5] in 1896. Subsequent reports have shown that corneal complications, although rare, may also occur.[3] Elschnig,[6] in 1897, reported 7 cases of molluscum contagiosum of the eyelids in 6 of which there was chronic conjunctivitis with multiple follicle formation closely resembling trachoma. The conjunctivitis disappeared after extirpation of the molluscum nodules. In a later report[3] Elschnig described a phlyctenular type of keratitis complicating the conjunctivitis. Gifford and Gifford,[7] in 1921, reported 6 cases of molluscum contagiosum of the eyelids in which there was secondary conjunctivitis. In 1 of these cases a corneal ulcer was present, which resisted ordinary treatment until the molluscum nodule

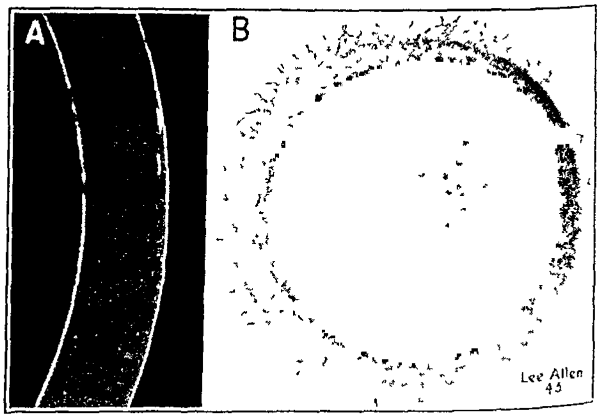

Fig. 1.—*A*, appearance of intraepithelial and subepithelial infiltrates with the narrow beam of the slit lamp; *B*, biomicroscopic appearance of corneal infiltrate.

was removed. Cavara[8] observed peripheral infiltration of the cornea, and a pannus-like lesion was described by Offret and Duperrat.[9] An unusual case was that reported by Quill,[4] in which a nodule of the lid was associated with a similar lesion of the cornea.

From the Department of Ophthalmology, State University of Iowa, College of Medicine.

1. Lipschütz, B.: Weitere Beiträge zur Kenntnis des Molluscum contagiosum, Arch. f. Dermat. u. Syph. **107**:387, 1911.

2. Juliusberg, M.: Zur Kenntnis des Virus des Molluscum contagiosum des Menschen, Deutsche med. Wchnschr. **31**:1598, 1905.

3. Elschnig, A.: The Significance of Molluscum Contagiosum as an Aetiological Factor of Conjunctival and Corneal Disease, Arch. Ophth. **51**:237, 1922.

4. Quill, T. H.: Molluscum Contagiosum of Eyelid and Cornea: Report of a Case, Proc. Staff Meet., Mayo Clin. **15**:139, 1940.

5. de Wecker: Klin Monatsbl. f. Augenh. **34**:64, 1896; cited by Gifford and Gifford.[7]

6. Elschnig, A.: Molluscum contagiosum und Conjunctivitis follicularis, Wien. klin. Wchnschr. **10**:943, 1897.

7. Gifford, H., and Gifford, S. R.: Molluscum Conjunctivitis, Arch. Ophth. **50**:227, 1921.

8. Cavara, V.: Le congiuntiviti da mollusco contagioso, Boll. d'ocul. **3**:1, 1924.

9. Offret, G., and Duperrat, R.: Les manifestations oculaires du molluscum contagiosum, Arch. d'opht. **2**: 993, 1938.

Thygeson,[10] in a recent paper on virus diseases of the eye, mentioned a case in which evere papillary conjunctivitis, superficial keraitis and pannus were associated with a molluscum nodule of the upper lid. The ophthalmia tealed promptly after excision of the nodule.

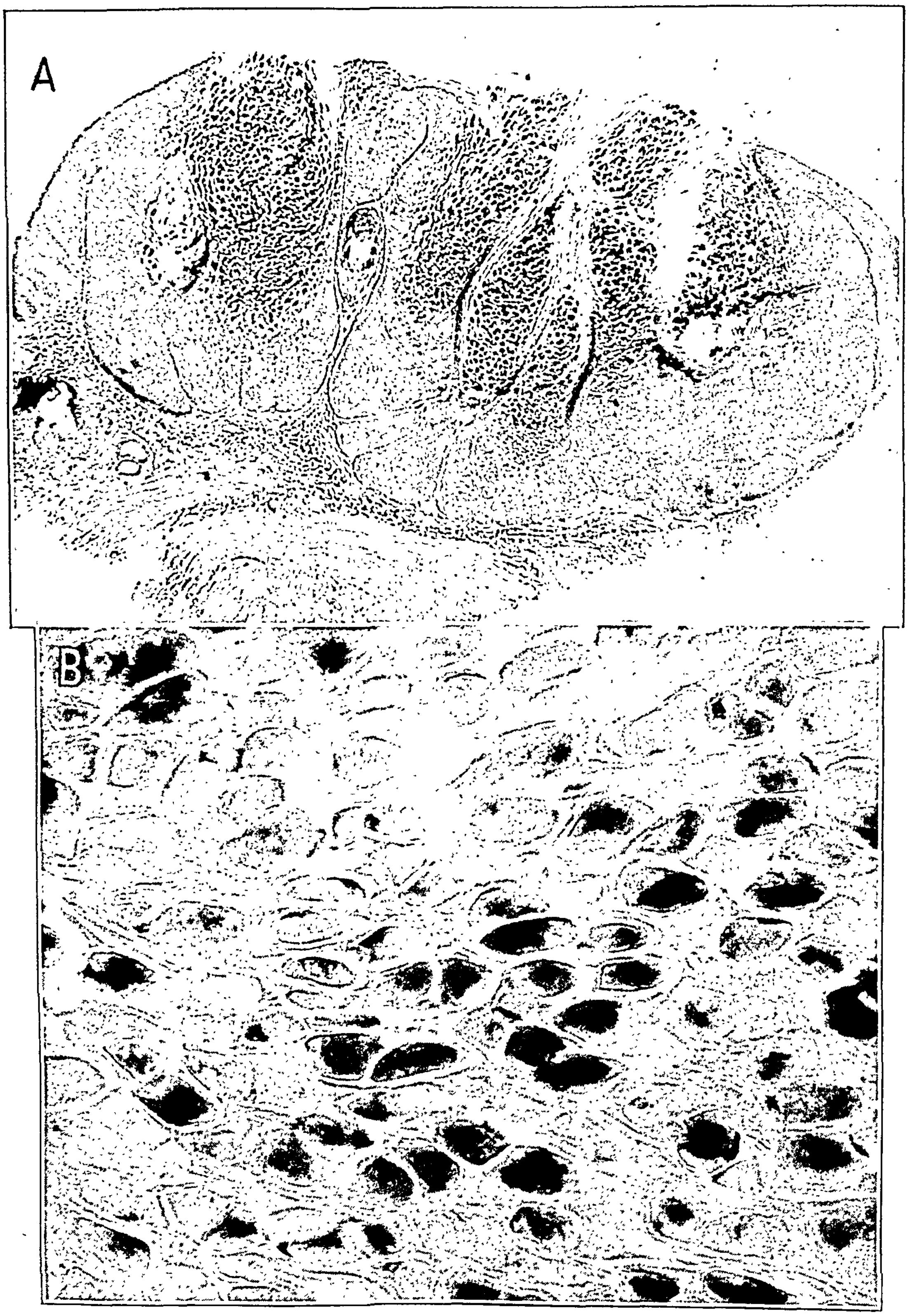

Fig. 2.—Photomicrographs of (*A*) a nodule of molluscum contagiosum (× 30) and (*B*) molluscum bodies (× 300)

REPORT OF A CASE

R. O., a man aged 24, was first seen in the ophthalmic clinic on Nov. 30, 1942, complaining of redness, slight itching, pain and crusting of the lid margins of the right eye during the past four days. The left eye was unaffected. Examination revealed the presence of diffuse hyperemia of the palpebral conjunctiva, which was more pronounced on the lower lid. There was a slight serous discharge. A tentative diagnosis of acute catarrhal conjunctivitis was made, and a collyrium composed of zinc sulfate, 0.25 per cent, in zephiran chloride (1 : 3,500) was prescribed. A forty-eight hour culture on blood agar of material from the conjunctival sac yielded no growth. The patient returned on December 5 with a number of flat conjunctival follicles in the lower cul-de-sac and a nontender, palpable preauricular gland. Because of the similarity of the condition to acute follicular conjunctivitis of the Béal type, the possibility of this disease was considered also. Culture of material on blood agar was repeated, but

10. Thygeson, P.: Viruses and Virus Diseases of Eye, Arch. Ophth. **29**:488 (March) 1943.

again no growth was obtained after forty-eight hours' incubation. Conjunctival scrapings stained with the Gram and the Giemsa technics revealed only a few epithelial cells with several monocytes and lymphocytes, but no organisms or inclusion bodies were seen. A collyrium containing isotonic solution of sodium chloride U. S. P. with epinephrine hydrochloride (1:1,000), 15 minims (0.93 cc.) to the fluid ounce (29.5 cc.), was prescribed, to be used three times a day. The patient returned, stating that he had improved under medication but that for the past three days there had been profuse lacrimation, severe photophobia, blepharospasm and the sensation of a foreign body in his eye. This was accompanied by slight pain and some blurring of vision.

Examination revealed the presence of edema and a large number of follicles in the conjunctiva of the lower eyelid and the inferior cul-de-sac. Also, a few follicles were seen in the conjunctiva of the upper eyelid in the canthal region. A faint circumcorneal flush was present. Examination with the biomicroscope showed the presence of a group of small subepithelial and intraepithelial corneal infiltrates, the latter staining faintly with fluorescein sodium (fig. 1). These infiltrates, eight to ten in number, were situated just nasal to the pupillary area of the cornea and had a diameter of about half that of a pinhead. Neither an aqueous flare nor floaters were observed in the anterior chamber. For the first time a small, round, yellow-tinged nodule, approximately 1.5 mm. in diameter, was seen on the margin of the lower lid. Umbilication could not be made out; yet the morphologic appearance of the lesion resembled that of a multilocular molluscum nodule. Nothing could be expressed from it by squeezing. It was thought to be either a nevus or a papilloma. Subsequent questioning of the patient revealed that the nodule had been noticed since the onset of conjunctivitis, five months previously, and that it had increased in size recently. Because of the absence of bacteria it was concluded that the condition was due to a virus infection. Its close similarity to epidemic keratonconjunctivitis in cases reported by Holmes,[11] Berliner [12] and others was noted. However, there was no edema of the lids or the bulbar conjunctiva, which is so characteristic of that condition. An attempt was made to culture the virus on the chorioallantois of the developing chick embryo, but without success. The results of culture and studies of smears were again negative. The patient was given phenocaine-epinephrine ointment and a pressure bandage to relieve ocular discomfort. Fifteen milligrams of riboflavin [13] was administered intramuscularly. This treatment was continued for five days, without any improvement in the patient's condition, and biomicroscopic examination revealed an increase in the number of subepithelial corneal infiltrates. The patient was referred to the department of dermatology, and a diagnosis of molluscum contagiosum was made. The nodule was then excised, and microscopic examination showed the typical histologic appearance of molluscum contagiosum (fig. 2). The patient's ocular complaints improved within twenty-four hours after removal of the nodule. In three days the subepithelial infiltrates could be distinguished only with difficulty, and when he was seen five days later, the patient was entirely free from ocular discomfort.

11. Holmes, W. J.: Epidemic Infectious Conjunctivitis, Hawaii M. J. **1**:11, 1941.

12. Berliner, M. L.: Epidemic Keratoconjunctivitis, Am. J. Ophth. **26**:50, 1943.

13. The riboflavin was given in the form of flavaxin niphanoid (Winthrop Chemical Company, Inc.).

COMMENT

Keratitis as a complication of molluscum contagiosum of the lid is rare, and the differential diagnosis may be difficult.

Although the occurrence of keratoconjunctivitis with molluscum contagiosum of the lid and its rapid cure following removal of the lesion may be known to many clinicians, it has received scant attention in the literature. The textbooks describe this disease as a disorder of the lid. No effect on the conjunctiva was mentioned by Norris and Oliver,[14] Ball,[15] Fuchs,[16] Atkinson,[17] Parsons [18] or Berens.[19] Conjunctivitis was noted by de Schweinitz,[20] Axenfeld [21] and Duke-Elder.[22] None of these authors described corneal involvement.

A review of the current literature showed that a conjunctivitis associated with molluscum contagiosum has been described by several authors. The condition is characterized by formation of follicles and sometimes papillary hypertrophy, at times so pronounced as to be confused with trachoma. In only 6 cases were corneal complications reported, and the lesions were all dissimilar.

The initial impression in the case reported was that of acute catarrhal conjunctivitis. Later, follicular conjunctivitis of Béal's type was considered since the early clinical characteristics of this condition were present—i. e., acute or subacute onset with much inflammation but little secretion; mild, nonpainful preauricular adenitis; absence of inclusion bodies or pathogenic bacteria, and presence of large mononuclear cells in conjunctival smears. The appearance later of corneal complications, however, made this diagnosis improbable. The resemblance of the subepithelial infiltrates to those appearing in cases of epidemic keratoconjunctivitis was noted and for a time it was believed the condition

14. Norris, W. F., and Oliver, C. A.: A Text-Book of Ophthalmology, ed. 2, Philadelphia, Lea Bros. & Co., 1900.

15. Ball, J. M., Jr.: Modern Ophthalmology, Philadelphia, F. A. Davis Co., 1904.

16. Fuchs, E.: Text-Book of Ophthalmology, authorized translation from the twelfth, revised and greatly enlarged German edition by A. Duane, ed. 8, Philadelphia, J. B. Lippincott Company, 1924.

17. Atkinson, D. T.: External Diseases of the Eye, Philadelphia, Lea & Febiger, 1934.

18. Parsons, J. H.: Diseases of the Eye, ed. 2, New York, The Macmillan Company, 1936.

19. Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936.

20. de Schweinitz, G.: Diseases of the Eye, ed. 10, Philadelphia, W. B. Saunders Company, 1924.

21. Axenfeld, T.: Lehrbuch und Atlas der Augenheilkunde, ed. 8, Jena, Gustav Fischer, 1935.

22. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2.

might be of this type. However, with the diagnosis of a molluscum nodule on the lid and rapid resolution of the keratoconjunctivitis following extirpation of the lesion, the cause of the ocular condition became evident. In this case the molluscum nodule was missed during the earlier days of treatment. Later, even when it had been seen, absence of the characteristic umbilication and inability to obtain any cheesy material on expression gave the impression that the lesion might be either a nevus or a papilloma. The difficulty in differential diagnosis of these three conditions has been pointed out by other observers.[23] The nodule may be definitely identified as that of molluscum contagiosum only when the presence of molluscum bodies can be demonstrated microscopically.

The mechanism of production of conjunctivitis and keratitis in cases of molluscum contagiosum is not yet clearly understood. Thygeson[10] expressed the belief that the desquamating material from the molluscum nodule contains a toxic substance which produces the inflammation.

In order that the possibility that a molluscum nodule is the underlying cause of a recalcitrant conjunctivitis or keratoconjunctivitis may not be overlooked, all nodules on the margins of the lids should be viewed with suspicion when they are associated with inflammation of the conjunctiva and cornea. Excision of such nodules for microscopic study should be done whenever possible.

University Hospital.

23. O'Brien, C. S., and Braley, A. E.: Common Tumors of the Eyelids, J. A. M. A. **107**:933 (Sept. 19) 1936. Quill.[4]

TUBEROUS SCLEROSIS

REPORT OF A CASE

ERNEST F. KRUG, M.D.

WITH THE ASSISTANCE OF FRANCIS A. ECHLIN, M.D.

NEW YORK

REPORT OF CASE

History.—G. R. a boy then 6 years old, was first brought to me in 1929 for removal of a facial rash and correction of the right upper eyelid. I noted that he had an angioma of the right upper lid, measuring about 6 by 10 mm., and that his face—both cheeks and the nose—was covered with a reddish brownish rash. Each small nodule apparently had a fine vascular loop. Careful ophthalmic examination, with instillation of drops, revealed that he was slightly far sighted; otherwise, his eyes were normal. The fundi were normal, and vision was 20/20 with a + 0.75 D. sphere.

He was referred to a dermatologist, but the diagnosis of adenoma sebaceum was not made. The dermatologist suggested electrolysis for removal of what was apparently a congenital lesion, but permission for this was refused.

I saw the patient again in 1936, when an examination of the eyes showed less hyperopia, clear media and normal fundi. The next examination was in November 1940. He had had some attacks of vertigo. The outlines of the disks were slightly blurred, but vision was 20/20 in each eye. Inspection of the visual fields gave no information. The possibility of a lesion of the brain led me to ask for a general neurologic and a roentgenologic examination. Permission for both was refused.

In March 1941 he was brought to me with the history of progressively severe headaches following epileptiform attacks, which had come on with increasing frequency.

In the interim he had been under the treatment of a rhinologist for a condition diagnosed as chronic sinusitis. He had lost a great deal of weight and looked in poor condition. Vision was reduced to 20/200 in the right eye and to 20/100 in the left eye. Examination of the fundi showed papilledema (3 to 4 D.) in both eyes, greatly contracted visual fields and a central color scotoma in the right eye.

I insisted on a roentgenographic and a neurologic examination, and the patient was referred to Dr. Francis A. Echlin, at the Lenox Hill Hospital. The neurologic examination showed that the boy was alert, well oriented and cooperative but irritable and somewhat facetious. There was no definite impairment of memory and no signs of aphasia. The sense of smell was intact. He was admitted to the Lenox Hill Hospital on March 5, 1941.

It was apparent that something must be done for him, as his fainting spells and headaches were becoming very frequent, appearing without warning and characterized by weakness and loss of control of the limbs and mental confusion. There was not complete loss of consciousness, and he displayed definite convulsive movements. Since January 1941 he had had several attacks of forceful vomiting.

There was no evident impairment of intellectual ability, but his speech had become thick and stumbling. Prior to 1940 he had been well and had attended school, and his grades were good. He had lost 40 pounds (18.1 Kg.) in weight.

Since birth there had been some rash on the face; this had developed gradually into a lesion of adenoma sebaceum. At the age of about 2 years the lesion was of the characteristic butterfly type, involving the sides of the cheeks and the nose.

Physical Examination.—The patient, now aged 17, was well developed. General physical examination revealed an essentially normal status except for several cutaneous lesions, the most extensive of which was a butterfly-shaped area involving the cheeks and nose (fig. 1). This lesion was adenoma sebaceum, similar to ones associated with tuberous sclerosis. A few nodules were present on the forehead at the hair line, and the chin was also somewhat involved. Another lesion, resembling that of the face and measuring 6 or 7 cm., was present in the lumbar region. The patient was alert, well oriented and cooperative but irritable.

The fundi showed complete obliteration of the margins of the disks, with about 4 D. of papilledema and scattered hemorrhages. There was no hemianopsia, but the visual fields were constricted for both form and color. The pupils were large but equal and regular and reacted to light and in accommodation. There was no nystagmus, and extraocular movements were normal. Upward gaze was not limited.

Neurologic Examination (Dr. Francis Echlin).—There was no facial asymmetry, and hearing was normal. The remaining cranial nerves were intact. Motor power was everywhere normal, and there was no atrophy or fibrillation. Muscular tone appeared good. Coordination was not affected. Gait was normal, and the patient walked without swaying. The sensory system was intact. The impression was that of an expanding intracranial lesion.

Since the absence of cerebellar or lateralizing signs and the history of sudden episodes suggested intermittent obstruction of the foramens of Monro or the aqueduct of Sylvius, a tumor of the third ventricle was considered, and the cutaneous lesion on the face made the diagnosis of tuberous sclerosis a possibility.

Roentgenographic Studies (Dr. Frank Huber).—Roentgenograms of the skull, taken on March 5, were reported on as follows: Some increase in intracranial pressure was manifested by a slightly greater prominence of the convolutional markings and slight separation of the coronal suture. The sella turcica was deepened, and there were some decalcification and atrophy of both the anterior and the posterior clinoid processes. Midway between the foramen magnum and the vertex, apparently slightly to the right of the mid-

From the Surgical Service of Lenox Hill Hospital.

Read at the Seventy-Ninth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 11, 1943.

line, were irregular, small areas of calcification within the structure of the brain. The pineal shadow was not definitely visualized. Small areas of increased density were scattered throughout the bones of the skull. The nasal accessory sinuses were rather extensively developed. There was no evidence of a pathologic condition. The right optic canal was slightly larger than the left

Ventriculographic Examination.—In view of the severe papilledema and the roentgenographic evidence, a ventriculographic examination was carried out in the usual manner. When the ventricular needle was passed into the posterior horn of the right lateral ventricle, clear fluid escaped under pronounced pressure. Fifty cubic centimeters of fluid was removed and replaced with air. A needle was then passed into the brain on the left side in the direction of the posterior horn of the lateral ventricle. At a depth of 4 cm. it entered a cavity containing canary yellow fluid. Twenty-five cubic centimeters of this fluid was removed and was replaced with 10 cc. of air. No air escaped when the needle was first placed in this cavity.

Since the cavity which was tapped in the left cerebral hemisphere contained yellow fluid and no air, the lesion must either have been a cyst or an obstruction of the left lateral ventricle so that it was no longer in communication with the right ventricle.

Roentgenograms taken at this time showed a small amount of air in the left lateral ventricle, with notable dilatation of the right lateral ventricle and a filling defect in the medial aspect of the floor of the body of this ventricle.

While the patient was on the x-ray table the ventricular needle was again placed in the left lateral ventricle, and 70 cc. of yellow fluid was removed and replaced with a smaller quantity of air. Roentgenograms taken at this time showed rather pronounced and fairly symmetric dilatation of both lateral ventricles (fig. 2).

A rounded filling defect measuring slightly more than 2 inches (5 cm.) in its anteroposterior diameter, was seen in each lateral ventricle near the junction of the body and the anterior horn The defect protruded into the ventricle from its inferior medial aspect. Small, irregular calcifications were seen in the defect on each side. There was no air in the third ventricle. The ventricular system did not show significant lateral displacement. The results of examination indicated that a mass blocked the foramens of Monro and probably obliterated the third ventricle. It also protruded into the anterior portions of the bodies of the lateral ventricles (fig. 2)

Fig 1.—Patient with adenoma sebaceum associated with tuberous sclerosis

Because of the location of the cerebral tumor and the probability that the condition was tuberous sclerosis, a difference of opinion arose as to the efficacy of surgical intervention, and operation was delayed forty-eight hours. Dr. Byron Stookey and Dr. Cornelius Dyke were called in consultation. They confirmed the location of the tumor and agreed that operation should be undertaken, especially since it was evident that the patient otherwise could not live more than a few weeks.

Operation (Dr. Francis A. Echlin).—On March 9 craniotomy and removal of the neoplasm were performed.

Before the dura was opened, it was noted that the brain was under considerable pressure. This was relieved by tapping the right lateral ventricle. When the dura was opened, numerous small, grayish plaques were visible in the cortex. These plaques did not deform the convolutions but appeared to be gliomatous.

On palpation, the cortex everywhere felt lumpy. There appeared to be normal areas of brain and many small, firm, whitish plaques, approximately 0.75 to 1.5 cm. in diameter. It was these plaques which gave the lumpiness to the cortex. Biopsy of this tissue was not made. A tumor was seen bulging from the region of the third ventricle into the medial wall of the right lateral ventricle, at the junction of the body and the anterior horn and in the region of the foramen of Monro. The medial wall of the neoplasm was bluish, and when the mass was opened, it was observed to contain soft tumorous tissue, resembling that seen in some medulloblastomas. This tumor was soft enough to be removed with ease by suction. After removal of the mass its medial, as well as its anterior, wall appeared to be surrounded by a capsule. When this capsule, which may have been the septum pellucidum, had been removed, one could see with ease into the left lateral ventricle and the anterior part of the third ventricle.

The choroid plexus appeared normal in both the right and the left lateral ventricle, and no other nodules on the walls of the ventricles were visible. The tumor

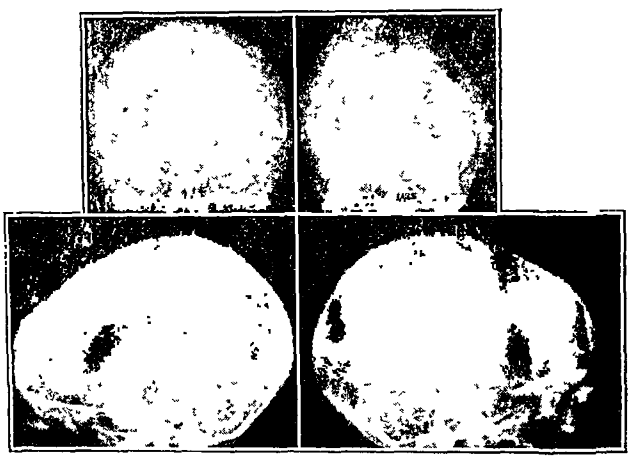

Fig. 2.—Roentgenograms of the skull in a case of tuberous sclerosis.

seemed to have been removed in its entirety. It apparently lay in the anterior part of the third ventricle and bulged upward and laterally into both lateral ventricles. It was approximately 2¼ inches (3 cm.) in diameter.

The patient left the table in fairly good condition. He was given a transfusion of 500 cc. of blood during the operation.

Microscopic Examination of Tumor (Dr. L. D. Stevenson).—Sections of the tumor were made at the department of pathology of Bellevue Hospital.

The material submitted contained a great deal of fibrous tissue (collagen) and in places groups of tumor cells, as illustrated in the sections. Nissl's method revealed that these cells often contained a nucleus and a well defined nucleolus. The cells were irregularly pear shaped—in many instances the cytoplasm trailed off into a process. Occasionally more than one process was visible. The cells resembled those seen in some of the nodular masses in the brain in cases of tuberous sclerosis (fig. 3).

Postoperative Course.—Convalescence was relatively smooth at first except for a rise of temperature to 105 F. on the day of operation. On the first postoperative day the temperature was 101.4 F.; the patient called me by name and moved the right arm and right leg freely on request. However, hemiplegia was present on the left side. On the third day after operation he was alert and rational; the decompression area was flat and pulsating, and the spinal fluid pressure on lumbar puncture had dropped to 140 mm. Left hemiplegia persisted, however. The course was one of slow improvement until March 22. There had been gradual return of motor power in the left arm and the left leg, and the patient was moving these extremities freely at this time. Power in the right arm and the right leg remained normal. There had, however, been fluctuations in the temperature to 103 F. during this period, but there was nothing to suggest infection of the wound, which had healed promptly, or of the spinal fluid.

On March 22 the patient became drowsy, and it was noted that he did not move any of his extremities. The temperature rose to 103 F. on March 24 and to 104 F. on March 25. For the next three weeks the course was stormy. It was believed that thrombosis of the longitudinal sinus had developed, perhaps at the time of operation as a result of traction of the brain on the sinus when the greatly distended ventricular system collapsed on the release of pressure. The patient became drowsy and almost completely out of contact with his surroundings. Generalized increase in tone developed in all the extremities, with loss of power, complete in the legs, bilateral grasp reflexes and a bilateral Babinski sign. During these three weeks there was irregular fever but no other sign of infection. He also began to have frequent attacks in which he showed the extensor rigidity of opisthotonos, with clenching of the fists (but not pronation of the wrists) and increase in the respiratory rate. These attacks occurred frequently when he was irritated and appeared more like a "sham rage" reaction than true decerebrate rigidity. In the intervals between attacks he was drowsy and irritable when questioned.

During his stay in the hospital he was given six roentgen treatments, with a total dose of 1,800 r, but the therapy was discontinued because of an unfavorable reaction.

Although the course of illness was still stormy, improvement began on April 3 and continued until his discharge from the hospital, on May 22. Power gradually returned to his arms. This improvement occurred first in the distal portion of the arms, and only later in the shoulder girdles. Power in the left leg also returned slowly, but there was little improvement in the function of the right leg. Visual acuity remained poor, and the disks showed pronounced secondary optic nerve atrophy. Mentally he became alert and well oriented. His conversation was intelligent, and he began to take a normal interest in his surroundings. Memory, however, remained imperfect.

It is now twenty-six months since operation. The patient is still confined to a wheel chair. His family believe that his mental state is about the same as before operation. He is alert, has a normal memory and takes a keen interest in his surroundings, in music and in world events. Judgment is perhaps impaired, and there is tendency to facetiousness. Motor power, as well as skilled movements, in the upper extremities is normal. There is moderate weakness of the left leg, but the right leg still shows considerable loss of power. He has had several minor attacks strongly suggestive of epileptic seizures, but none has occurred since he

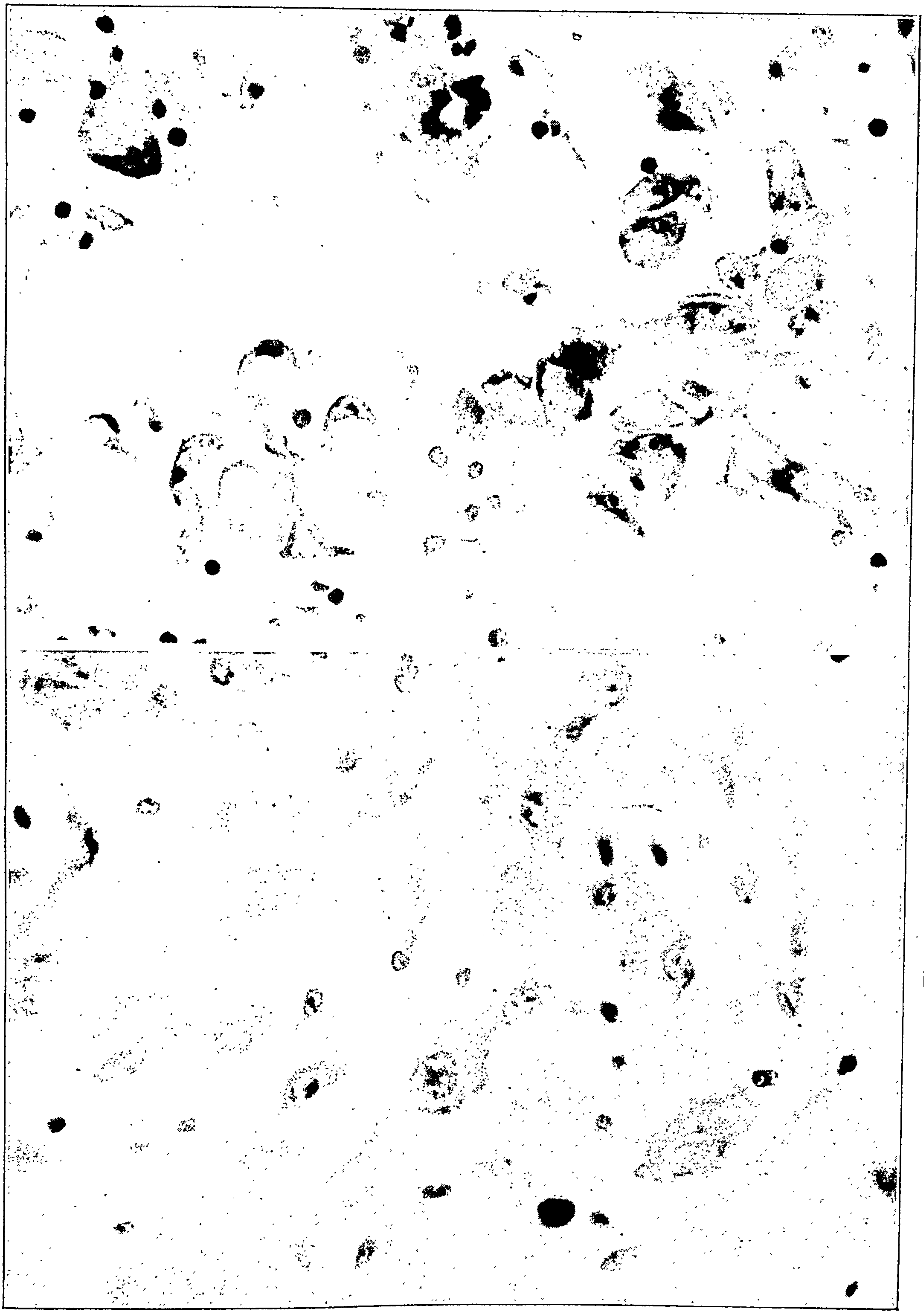

Fig. 3.—Microscopic sections of the tumor in a case of tuberous sclerosis.

was placed under sedation with phenobarbital, nine months ago.

Visual Acuity.—At the last examination both disks were dead white, with blurred edges. There was secondary nerve atrophy. The patient had light perception in the right eye, and vision was approximately 20/50 in the left eye, with ability to read Jaeger type 7. He read the headlines of the newspaper slowly. The left visual field showed concentric contraction to about 20 degrees.

COMMENT

Tuberous sclerosis is a disease entity. The term was first used by Bourneville to describe a rare form of cerebral sclerosis, which occurred chiefly in children and young persons. Neurath's oldest patient was 35 and Vogt's 37 years old, but a rare case of the disease occurring at the age of 75 was reported by Niewenhuijse.

Vogt,[1] in 1908, established the clinical syndrome of mental deficiency, epilepsy and adenoma sebaceum. After the work of Vogt, many other cases were reported, and it became evident that incomplete forms of the syndrome may occur. It was recognized that the cerebral condition might exist in the absence of one, or even all, of the other clinical signs.

Tuberous sclerosis appears to be more frequent in European countries; almost all subjects have been of the white race, Jews and Gentiles being affected alike.

Adenoma sebaceum, or nevus sebaceus, is a disease of congenital origin, which in our case appeared early, but it may not become evident until adolescence; it is characterized by pinhead-sized, yellow or reddish, waxy papules, situated on the flush areas of the face. The rash seen in the present case of tuberous sclerosis was of the Pringle type. In this type the blood vessels are especially affected, the lesion being essentially an increase in the size of the sebaceus glands, accompanied by proliferation of connective tissue and increased vascularity. As in our case, dermatologic lesions may appear on the trunk or the extremities.

Tuberous sclerosis is so named because of the potato-like appearance of the morbid growth. Neoplasms of this type may appear in the kidney, the heart, the lungs, the spleen and the retina.

Schuster,[2] in 1913, described a case of tuberous sclerosis with adenoma sebaceum in a young man who was of normal intellect but was subject to epileptiform attacks. He also reported a case in which a youth aged 16 manifested adenoma sebaceum, epilepsy and signs of intracranial tumor during life. Autopsy revealed tuberous sclerosis with multiple renal tumors.

The signs of intracranial tension are evident in early adult life. The epileptiform attacks, in the form of petit mal, may be present for many years without gross mental defect. Involvement of the third ventricle is reported in most of the cases of increased intracranial pressure. The epileptiform seizures are an important symptom, both in typical and in atypical cases. All types of attacks may be encountered—grand mal, petit mal, jacksonian convulsions, fainting spells without convulsions and paroxysmal outbursts—but in the absence of all these manifestations a facial eruption should arrest the attention and suggest the presence of tuberous sclerosis. Papilledema at once suggests intracranial neoplasm. Experience in the present case indicates that if a surgically accessible tumor is shown in the encephalogram, its successful removal should prolong the life of the patient and relieve him of his headaches and other unpleasant symptoms.

Associated retinal tumors are comparatively rare (van der Hoeve[3]). The pathology of tuberous sclerosis is not discussed in this preliminary report. With Dr. Echlin, I hope to submit a further report after a few years' observation of this patient. The patient is still an invalid, and the question arises how much usefulness he will recover eventually. The literature has many excellent reports on this subject. Messinger and Clarke,[4] Globus, Strauss and Selinsky[5] and van der Hoeve[3a] described the pathologic conditions in the eye.

Tuberous sclerosis is an endogenous, hereditary disease. Its relation to general neurofibromatosis is frequently pointed out, but Niewenhuijse opposed this concept, expressing the belief that the two conditions were different not only in their clinical manifestations but in their ana-

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3. (*a*) van der Hoeve, J.: Augengeschwülste bei der tuberösen Hirnsklerose (Bourneville), Arch. f Ophth. **105**:880-898, 1921; (*b*) Eye Diseases in Tuberous Sclerosis of the Brain and in Recklinghausen's Disease, Tr. Ophth. Soc. U. Kingdom **43**:534-541, 1923.

4. Messinger, H. C., and Clarke, B. E.: Retinal Tumors in Tuberous Sclerosis: Review of the Literature and Report of a Case, with Special Attention to Microscopic Structure, Arch. Ophth. **18**:1-11 (July) 1937.

5. Globus, J. H.; Strauss, I., and Selinsky, H.: Das Neurospongioblastom, eine primäre Gehirngeschwulst bei disseminierter Neurospongioblastose (tuberöse Sklerose), Ztschr. f. d. ges. Neurol. u. Psychiat. **140**: 1-29, 1932.

tomic changes. He stated that the tumors in the brain are small glial foci in the cortex, which have their counterpart in the occasional fibromas associated with tuberous sclerosis. Surely the picture is dependent on a congenital disturbance in the development of the undifferentiated neuro-epithelial cells, which, according to the location in which they begin to grow—the central, the peripheral or the sympathetic nervous system—give rise to tuberous sclerosis or to neurofibromatosis or to a combination of the two conditions. Bielschowsky spoke of neurinomatosis centralis peripherica universalis. Reese [6] submitted an excellent article on the relation of tuberous sclerosis to drusen of the optic nerve, and Loewenstein and Steel [7] discussed the retinal lesions in this condition.

988 Fifth Avenue.

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6. Reese, A. B.: Relation to Drusen of Optic Nerve to Tuberous Sclerosis, Arch. Ophth. **24**:187-205 (July) 1940.

7. Loewenstein, A., and Steel, J.: Retinal Tuberous Sclerosis (Bourneville's Disease). Am. J. Ophth. **24**: 731-741, 1941.

PUPILLOGRAPHIC STUDIES

V. PERIODIC SYMPATHETIC SPASM AND RELAXATION AND ROLE OF SYMPATHETIC NERVOUS SYSTEM IN PUPILLARY INNERVATION

OTTO LOWENSTEIN, M.D.
NEW YORK
AND
LIEUTENANT ARNOLD S. LEVINE (MC), U.S.N.R.

The syndrome of alternating spastic and paretic phases of a periodic (cyclic) nature in paralysis of the third cranial (oculomotor) nerve has frequently been observed since it was first described by Rampoldi, in 1884. In 1942 Lowenstein and Givner,[1] on the basis of pupillographic studies, showed that there is no real paralysis of the sphincter muscle and suggested therefore that the syndrome be spoken of no longer as a cyclic oculomotor paralysis but as an intermittent spasm of the third nerve with irregular periodicity (periodic spasmus mobilis oculomotorii). They showed that it is the result of partial destruction of the nucleus for the sphincter of the iris combined with supranuclear lesions, involving particularly the connections between the nucleus for the sphincter and the hypothalamus.

In contrast to this, periodic spasm of the sympathetic pupillary innervation has, to our knowledge, never been reported. In 1907 Westphal[2] described the phenomenon of transitory pupillary immobility to light and to near vision in cases of catatonia and hysteria and, later, in postencephalitic states. He observed that in a certain number of cases of catatonia this phenomenon was displayed: The pupil becomes dilated and no longer reacts either to light or in near vision. Such a phase of immobility may last for seconds, hours or even days. One of us (O. L.)[3] showed in 1920 that the phenomenon is of true sympathetic origin, since the spasms may be produced by such psychologic stimuli as pain and fear, which result in a long-lasting state of anxiety, common in catatonic and hysterical persons; it can, however, be observed in some normal persons of characteristic constitution (Bumke's anxiety pupils). Westphal later called this phenomenon spasmus mobilis pupillae. One of us (O. L.)[3] showed that it could regularly be abolished when the state of anxiety was allayed by suggestion of other emotions, such as joy. This spasmus mobilis of Westphal never showed a periodic nature.

The phenomenon we wish to describe is quite different from Westphal's spasmus mobilis. In particular, it is independent of psychologic conditions and is periodic.

REPORT OF A CASE

An unmarried girl aged 22 was first seen by one of us (A. L.) in the neurologic service of Dr. S. P. Goodhart at Montefiore Hospital. The family history, the history prior to onset of the present illness and the psychosocial history were noncontributory.

From the Department of Neurology, New York University College of Medicine.

This study was aided by grants from the Altman Foundation and the Oberländer Trust.

1. Lowenstein, O., and Givner, I.: Cyclic Oculomotor Paralysis (Spasmus Mobilis Oculomotorius), Arch. Ophth. **28**:821-833 (Nov.) 1942.
2. Westphal, A.: Ueber bisher nicht beschriebene Pupillenerscheinungen im katatonischen Stupor, Allg. Ztschr. f. Psychiat. **64**:694, 1907.
3. Lowenstein, O.: Experimentelle Beiträge zur Lehre von den katatonischen Pupillenveränderungen, Monatschr. f. Psychiat. u. Neurol. **47**:194, 1920

Previous Course of Illness and Examinations.—On the patient's first admission to the hospital, on Sept. 16, 1936, at the Neurological Institute of New York, her complaints consisted of "progressive weakness of the muscles of the left arm and shoulder, occasional aching pain in the left shoulder and elbow joint, inability to straighten the left elbow joint completely and excessive sweating of the little finger of the left hand of two years' duration."

Physical examination at that time revealed well defined asymmetry of the two halves of the body, the left side being smaller than the right; a transient Horner syndrome on the left side; excessive sweating of the left side of the face with pilocarpine; almost constant excessive sweating over the distribution of the left ulnar nerve; a positive "manual Babinski" reflex [4] on the left; slight hypesthesia over the deltoid region of the left arm, and slight hyperreflexia of the left lower extremity.

The results of laboratory studies, including hematologic examination, urinalysis, examination of the spinal fluid, serologic tests and determination of the basal metabolic rate, were all within normal limits. Roentgenographic studies showed the presence of bilateral cervical ribs (larger on the right side than on the left) and a normal spine; an air encephalogram revealed nothing abnormal. Examination of the eyes on September 22, and again on October 9, disclosed a Horner syndrome on the left side. The patient was discharged for follow-up study after five weeks of hospitalization.

On second admission to the same hospital, on Dec. 8, 1936, the patient complained, in addition to the aforementioned disturbances, of a sensation of stiffness in the left arm and the left leg. She had been receiving roentgen therapy through the outpatient department. Examination now revealed excessive sweating over the left side of the face and in the palm of the left hand. The ophthalmologist reported that the "right pupil was still larger than the left." While the "reflexes in the left lower extremity were more active than those in the right," the reflexes in the right upper extremity "were a trifle more active than those in the left." There was an indefinite area of hypalgesia and hypesthesia over the left deltoid region. The other physical findings were the same as before.

The manometric reading of the spinal fluid now showed an initial pressure of 246 mm. (water manometer), with normal responses to jugular compression. After removal of 10 cc. of spinal fluid the pressure was 160 mm. She was again discharged.

The patient was again admitted to the Neurological Institute of New York on March 11, 1937, with the report of steady progression of symptoms. Now she definitely favored her right lower extremity when walking, and associated movements in the left upper extremity were diminished. There was decided weakness in extension and flexion of the left elbow and in abduction and adduction in the left shoulder. Babinski and Oppenheim signs were reported on the left side, with diminished abdominal reflexes on the same side. The other findings were the same as before, except that the sensory changes over the left deltoid region were no longer present. The results of laboratory studies were again within normal limits, with the protein content of the spinal fluid 23 mg. per hundred cubic centimeters.

On April 10 a cervical laminectomy (third to sixth cervical vertebra) was performed. The surgeon expressed the opinion that there was a "firm intramedullary tumor" at the lèvel of the third to the sixth cervical neural segment. He was unable to rotate the cord and reported that on palpation "the entire cervical portion of the cord was extremely resistant." The cord was not split, and no material was taken for biopsy. The patient was discharged on May 7.

A fourth admission to the same hospital took place on June 1, 1937 because, toward the end of May, the patient began to walk "with shaking of the entire body" and numbness developed over the head and neck and between the shoulder blades. Physical examination now revealed a peculiar "undulating" gait, inability to perform equilibratory tests, dysmetria and asynergia in both heel to knee tests. In addition, there was adiadokokinesis on the left side. There was bilateral ankle clonus, with increased patellar and suprapatellar reflexes. Plantar responses were absent.

Her next admission was to the Brooklyn Jewish Hospital, on Feb. 8, 1938. Here the report indicated that "the left pupil was smaller than the right, the left palpebral fissure narrower than the right and the left eye slightly less prominent." Weakness was noted in both upper extremities (greater in the left than in the right), in the trunk muscles and in both lower limbs (greater in the left than in the right). There was a positive Romberg sign. The reflexes in the left lower limb were increased; the lower abdominal reflexes were absent, and an extensor response to plantar stimulation was noted on the left side. The patient was given another course of roentgen therapy. However, despite therapy, her condition became progressively worse.

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4. Pool, J. L.: Manual Reflex: The Ulnar Adductor Reflex, Bull. Neurol. Inst. New York **6**:372-377, 1937.

Present Study.—She was admitted to the Montefiore Hospital on June 18, 1939. Examination at this time revealed a decided limp, with dragging of the left lower extremity. The left elbow was usually held in flexion, and there was a marked defect in the swing of the left arm. It was noted then that the fingers of the left hand were usually held in flexion but at times would straighten slowly and then flex again. A main en griffe was described. A Horner syndrome was present on the left. In addition, hyperalgesia was noted from the fourth lumbar to the second sacral dermatome on the left and, to a somewhat less marked degree, from the fifth lumbar to the second sacral dermatome on the right. The results of the rest of the examination were similar to those previously reported. Subsequent studies revealed that instillation of cocaine into the eyes caused dilation of both pupils, more on the left side than on the right. After a course of roentgen therapy, the patient appeared stronger; the few sensory changes disappeared, and she was discharged to the outpatient department. The results of laboratory studies were within normal limits. Definite improvement in gait was noted.

For one year her condition remained stationary, until about September 1941, when subjective weakness recurred in the left leg, as well as in the right arm. She was readmitted to Montefiore Hospital on Dec. 11, 1941. A peculiar gait was then described in which, with each step on the left side, the knee would buckle under and then would seem to catch itself and straighten out. The patient showed a tendency to walk mostly on the ball of the left foot. In addition, a "glove and stocking" type of sensory disturbance was noted on the left side, with hypesthesia, hyperalgesia and dysalgesia, dysthermesthesia and hypthermesthesia to both cold and to heat over the involved areas.

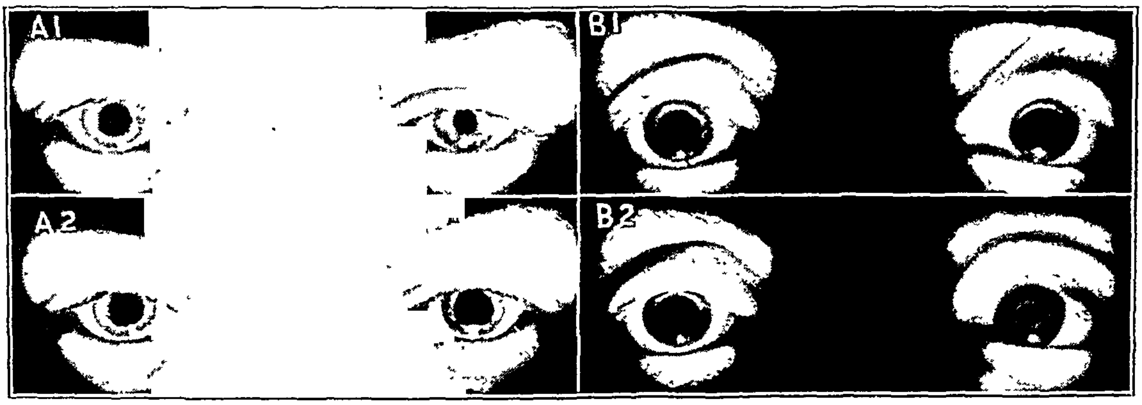

Fig. 1.—*A*, periodic sympathetic spasm and relaxation of the pupil. *1*, phase of sympathetic paresis when the left pupil is small. *2*, phase of sympathetic spasm when the left pupil is large. In *2* the palpebral fissure is widened as compared with that shown in *1*.

B, cyclic spasm and paralysis of the third nerve. *1*, phase of paralysis when the left pupil is large. The left upper eyelid is in ptosis and was held open by hand. *2*, phase of spasm when the pupil is small. The left eyelid opened spontaneously.

A tendency to flexor spasm of the ulnar three fingers on the left hand was noted. Other findings were hyperreflexia in the right upper and the left lower extremity and patellar and ankle clonus on the left side. Pathologic reflexes were definite on the left side and equivocal on the right side.

In January 1942 the ocular phenomenon to be described in detail later was first noted by one of us (A. L.) and has been studied exhaustively. The spasms of extension at the wrist and flexion of the ulnar three fingers occurring at irregular, but frequent, intervals were observed to become more intense and more frequent. These spasms were seen both in association with ocular changes (fig. 1 A_1 and A_2), preceding them by ten to twenty seconds, and independently. The reverse, i. e., ocular changes without the spastic contractions in the left hand, were never observed. Tests for sweating revealed no abnormalities, despite all previous subjective reports and objective observations. Studies of cutaneous temperature confirmed the gross observation that the left hand was warmer than the right and that the right foot was warmer than the left. Histamine tests (intradermal) revealed absence of the flare (loss of axon reflex) in the left foot and marked diminution of the flare in the left hand. The mecholyl chloride test (intradermal) revealed a much greater reaction in the right foot than in the left and a greater reaction in the left hand than in the right. Reflex changes in cutaneous temperature with the feet immersed either in hot or in cold water, under control, were normal on the left side and were greatly diminished on the right side.

The neurologic diagnosis was intramedullary disease of the cord, degenerative in character, most likely syringomyelia. The history, progress and present clinical picture spoke against the presence of neoplasm.

PUPILLOGRAPHIC STUDIES

1. PERIODIC DILATION OF THE LEFT PUPIL

The left pupil underwent periodic dilation five to twenty seconds after the beginning of a spastic extension of the left wrist combined with flexion of the third, fourth and fifth fingers of the left hand. When the pupil began to dilate, the hand was already in a state of spasm. The pupillary spasm was never observed except when preceded by spasm of the hand and fingers. However, spasm of the hand developed without an ensuing pupillary spasm about once in twenty-five reactions.

A. Dilation Without Application of Drugs.—The periodic dilation occurred about once every five minutes; it consisted of the following phases:

1. A preliminary phase of very slow dilation, lasting about 1 to 1.5 seconds, with an extent of about 0.2 mm. and an average speed of 0.16 mm. per second.

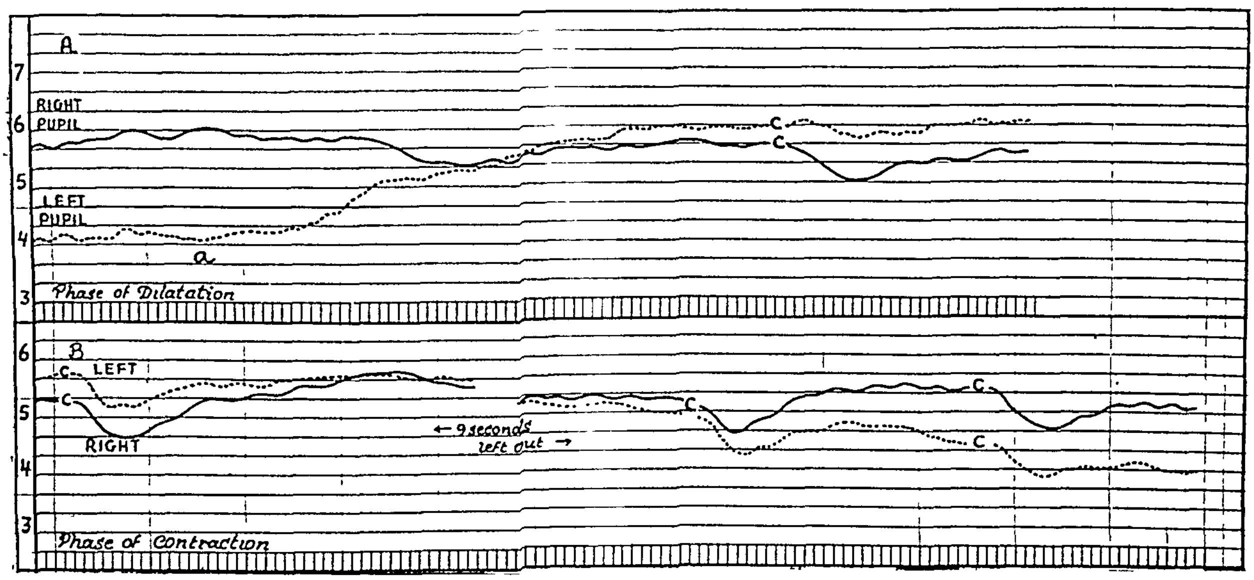

Fig. 2.—Spontaneous dilation and contraction of the left pupil.

A, phase of dilation beginning at *a*. *B,* phase of contraction. The continuous course of the curves is interrupted by several spontaneous lid closure reflexes (*c,* contraction and redilation). The lid closure reflex of the left pupil was diminished during the phase of dilation and increased as soon as active dilation was completed.

2. A primary stage of rapid dilation lasting about 1.4 to 1.6 seconds, with an extent of about 1.55 mm. and an average speed of 1 mm. per second.

3. A secondary phase of slow dilation, lasting about 2 to 3 seconds, with an extent of 0.2 to 0.3 mm. and an average speed of 0.1 mm. per second.

The maximal dilation was sustained about 5 seconds. Then a very slow contraction, lasting about 30 seconds, began. After approximately 15 seconds the left pupil was of about the same diameter as the right pupil, remaining at this level for about ten seconds. The left pupil then continued to contract beyond the extent of the right pupil for about 5 seconds longer, until it was about 1 mm. smaller. Closure of the lids during the primary phase called forth a normal reflex contraction of the right pupil; in the left pupil, however, it only retarded the pupillary dilation. A real closure reflex of the lid was not produced until the maximal pupillary dilation was reached, and was even then diminished.

When a light stimulus struck the eye during the period of active dilation, the light reflex elicited was less than during the phases in which the left pupil was either small or large. When, however, a light stimulus struck the eye during the period of active contraction, the light reflex elicited was greater than at any other time.

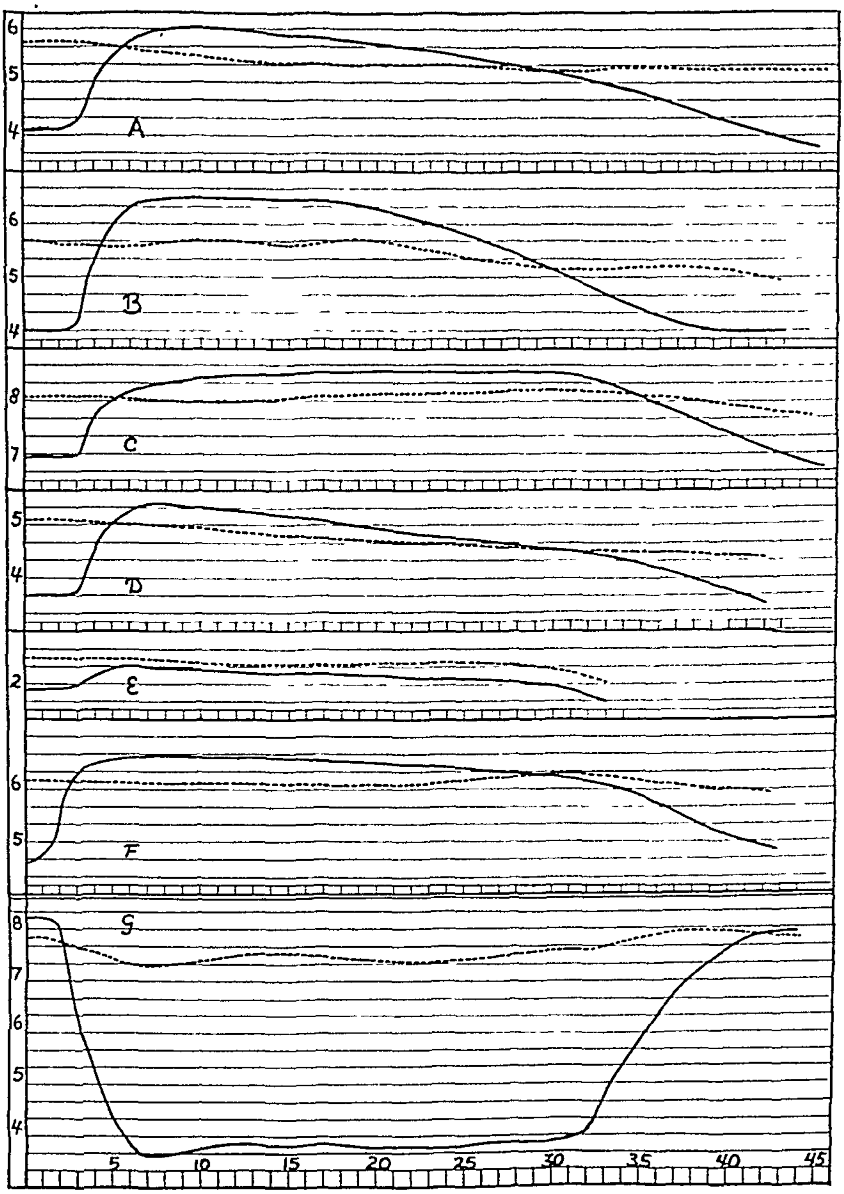

Fig. 3.—Spontaneous dilation and contraction of the left pupil without drugs and under the influence of drugs.

A, without drugs. *B*, fifteen minutes after the instillation of cocaine into the conjunctival sac. The speed and extent of dilation are slightly increased. The period of spastic dilation is prolonged. The rate of contraction is also increased. *C*, fifty-five minutes after the instillation of cocaine into the conjunctival sac. The pupillary diameter has increased to 6.8 mm. The period of spastic dilation is further prolonged. *D*, twenty-three minutes after the instillation of physostigmine into the conjunctival sac. The pupillary diameter has decreased to 3.7 mm. from its original 4.1 mm. The speed of dilation is not affected. The period of spastic dilation is slightly shortened. The preliminary phase of dilation, however, is absent. *E*, thirty-five minutes after the instillation of physostigmine into the conjunctival sac. The pupillary diameter has further decreased to 1.9 mm. The preliminary phase of dilation is absent. The average speed of dilation is decreased to 0.15 mm. per second. The period of spastic dilation is also decreased. *F*, effect of epinephrine. *G*, spontaneous contraction and dilation of the pupil in a case of periodic spasm of the third nerve (for comparison).

B. Dilation Under Influence of Drugs (fig. 3).—Cocaine Hydrochloride: Fifteen minutes after the instillation into the conjunctival sac of 3 drops of 1 per cent solution of cocaine hydrochloride the preliminary and primary phases were slightly accelerated but were not increased in extent. In the secondary phase, however, both the extent and the speed of dilation were increased to about twice their previous values (table). Forty minutes later, when the diameter of the pupil had increased from 4.2 to 6.8 mm., all stages of the periodic dilation were again decreased.

Dilation of the Left Pupil Without Drugs and After Application of Cocaine and Physostigmine

Condition	Pupillary Diameter, Mm.	Preliminary Phase of Dilation			Primary Phase of Dilation			Secondary Phase of Dilation			Total Dilation		
		Extent, Mm.	Duration, Sec.	Speed, Mm./Sec.	Extent, Mm.	Duration, Sec.	Speed, Mm./Sec.	Extent, Mm.	Duration, Sec.	Speed, Mm./Sec.	Extent, Mm.	Duration, Sec.	Speed, Mm./Sec.
Without drugs............	4.1	0.2	1.0-1.5	0.16	1.55	1.4-1.6	1.0	0.3	2.0-3.0	0.1	2.05	5.25	0.4
Cocaine													
After 15 minutes.......	4.2	0.2	1.0	0 2	1.55	1.4	1.1	0.7	3.0	0.23	2.45	5.4	0.45
After 55 minutes.......	6.8	0.1-0.2	1.0	0 15	0.8	1.3	0.61	0.4	3.0	0.13	1.35	5.3	0.25
Physostigmine													
After 23 minutes.......	3.7		Absent		1.2	1.5	0.8	0.5	2.7	0.19	1.7	4.2	0.4
After 35 minutes.......	1.9		Absent		0 35	1.5	0.23	0.2	2.2	0.09	0.55	3.7	0.15

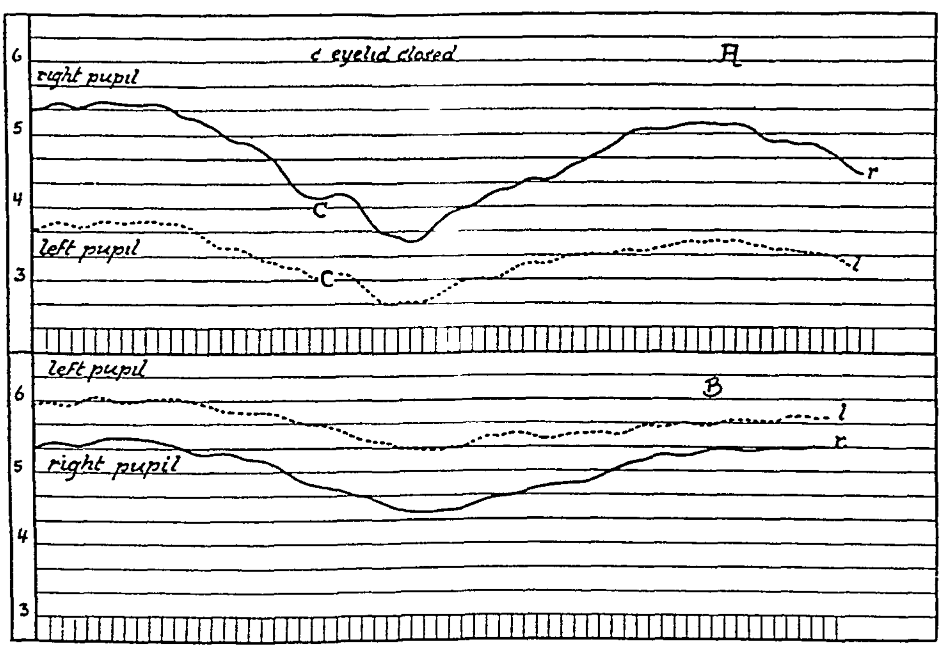

Fig. 4.—Nonperiodic spontaneous movements of both pupils.

A, when the left pupil is small; *B*, when the left pupil is large. Superimposed lid closure reflexes are represented by *c*. The spontaneous movements appear to be more extensive in *A* than in *B*.

2. Physostigmine Salicylate: Under the influence of physostigmine salicylate the preliminary phase disappeared entirely, and the primary and secondary phases decreased in speed, although not in duration.

Epinephrine Hydrochloride: The reaction was like that to cocaine, but to a lesser degree.

II. OTHER SPONTANEOUS PUPILLARY MOVEMENTS

Besides the so-called spastic periodic movements already described, both pupils performed other spontaneous movements. These were very slow vermiform contractions, occurring simultaneously in the left and in the right pupil.

In the right pupil they consisted of contractions about 1.5 mm. in extent at a speed of 1.3 mm. per second. When the left pupil was small, they consisted of contractions about 1 mm. in extent at a speed of 0.75 mm. per second. In the spastic phase of the left pupil, that is, when the pupil was large, they consisted of contractions of about 0.7 mm. in extent at a speed of 0.3 mm. per second. That is, these spontaneous movements were slower in the large than in the small phase of the left pupil (fig. 4). It appears, furthermore, that these spontaneous movements were less sluggish (0.49 mm. per second) when both pupils were under constant illumination than when they were in complete darkness. These movements involved both pupils and may be considered hippus.

Under the influence of cocaine, these spontaneous movements diminished both in frequency and in extent and finally disappeared after the pupillary diameter had reached more than 7 mm. Under the influence of physostigmine, however, they persisted, even tending to become less sluggish when the drug was beginning to take effect (after twenty-five minutes). They also persisted under the influence of epinephrine.

After the pupil had contracted to a diameter of 2.5 mm., the hippus became very sluggish in the left pupil and somewhat sluggish in the right pupil; it amounted in the left pupil to only 0.3 mm. at a speed of about 0.3 mm. per second and in the right pupil to 0.5 mm. at a speed of 0.5 mm. per second.

III. REACTION TO LIGHT

A. Without the Use of Drugs.—Both pupils reacted to light both directly and consensually. There were, however, characteristic differences between the two pupils, both when the left pupil was large and when it was small.

In analyzing the reflexes to light, one must bear in mind the fact that in normal reflexes to light the contraction follows a latent period of about two-tenths to three-tenths second. The contraction period consists of three phases: a primary phase of about 0.3 to 0.4 second and an average speed of about 5.5 mm. per second; a secondary phase of about 0.3 to 0.4 second and an average speed of about 2 mm. per second, and a tertiary phase (which is variable) of about 0.3 to 0.5 second and an average speed of 0.8 to 1.9 mm. per second. The whole contraction is carried on with an average over-all speed of 2.5 mm. per second (fig. 5).[4a]

We first state that in the case in question all speeds were far below these values both as to the primary and as to the secondary and tertiary phases of contraction.

4a. Gradle and Eisendrath (Klin. Monatsbl. f. Augenh. **71**:311-313, 1923) and Gradle and Ackerman (Reaction Time of the Normal Pupil, J. A. M. A. **99**:1334-1336 [Oct. 15] 1932) distinguish a primary and a secondary phase of contraction, the former appearing identical with our primary contraction phase, while the latter seems to include our secondary and tertiary contraction phases. They found a latency of 0.1875 second, a primary contraction phase of 0.4365 second at an average speed of 5.48 mm. per second and a secondary contraction phase of 0.3125 second at an average speed of 1.34 mm. per second. The whole contraction amounted to 2.82 mm.

with only one exception, the direct reaction of the right pupil, the primary contraction phase of which showed an average speed of 5.3 mm. per second. This is within the limits of normal. Secondary and tertiary phases of contraction in this case were below the normal values, although the speed of the whole contraction was still within the limits of normal.

The consensual reaction of the right pupil was approximately the same whether the directly stimulated left pupil was small or large. The time of contraction as

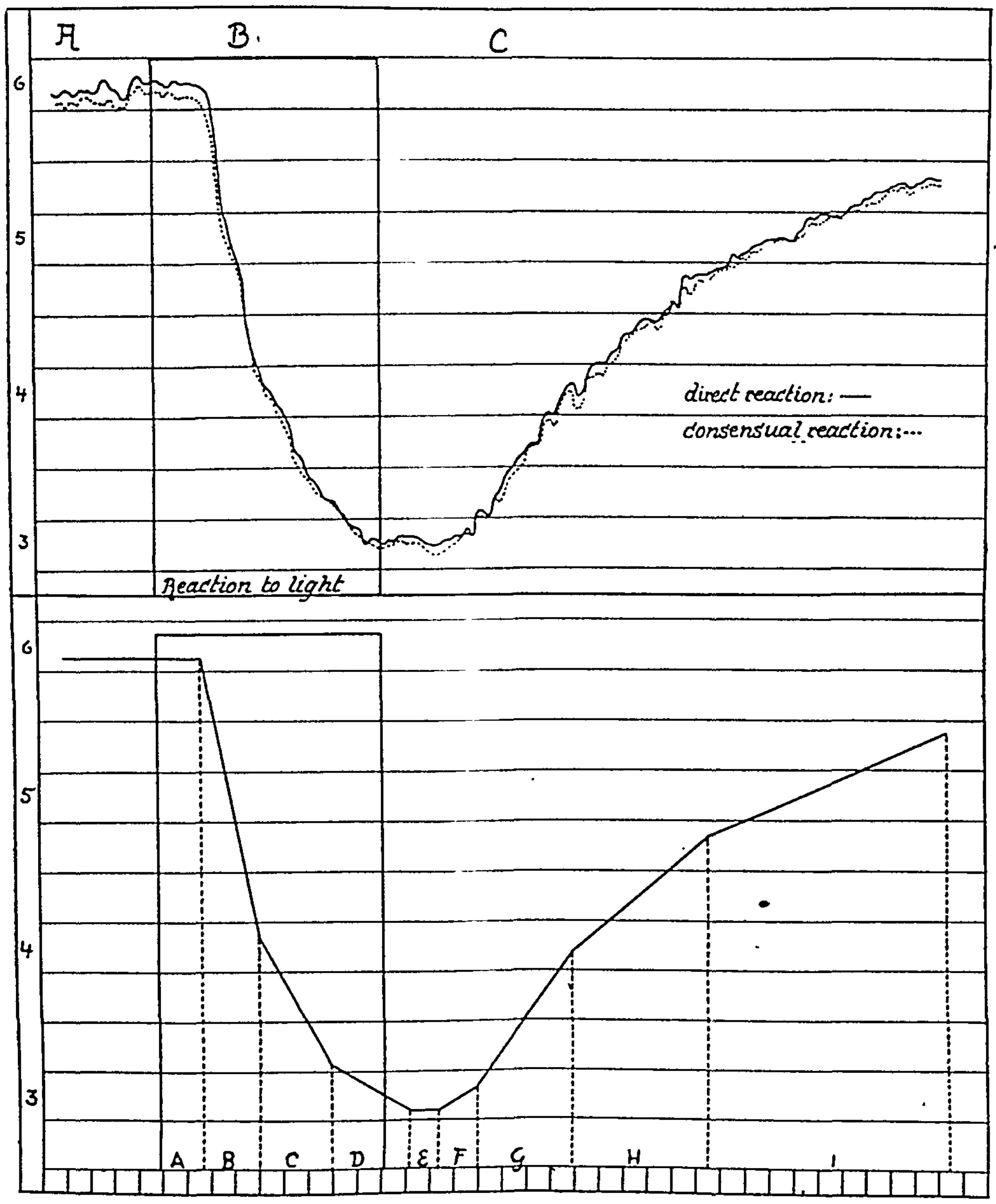

Fig. 5.—The normal reflex to light; method of interpretation.

First graph: *A*, pupils adapted to darkness, before stimulation with light. Note pupillary unrest. *B*, application of light stimulus (nine-tenths second) to one eye. Both pupils contract after a latent period. *C*, termination of light stimulus. Both pupils redilate after a second latent period.

Second graph (method of interpretation): *A*, latent period of contraction; *B*, primary phase of contraction; *C*, secondary phase of contraction; *D*, tertiary phase of contraction; *E*, latent period for redilation; *F*, preliminary phase of redilation; *G*, primary phase of redilation; *H*, secondary phase of redilation, and *I*, tertiary phase of redilation.

compared with that of the normal pupil was high, and the speed of the contraction was low; both values, however, were still within the limits of normal.

When the left pupil was small, its primary phase of contraction was normal; the secondary phase was decreased in extent, but not in duration, and the tertiary phase was absent.

When the left pupil was large, its primary phase of contraction was about equal to that of the same pupil when small, while the secondary phase was more extensive and the tertiary phase even longer and more extensive than the normal (fig. 6).

The consensual light reactions of the left pupil in all phases of contraction were equal to the direct reactions, both in the large and in the small phase.

The total contraction time was prolonged in both pupils.

B. With Cocaine (fig. 7).—1. Small Phase of Left Pupil: The direct reaction of the left pupil was not altered in its primary phase, but went on at a much higher speed and to a greater extent in its secondary and tertiary phases.

2. Large Phase of Left Pupil: The reactions of the left pupil slowed down and became less extensive in all phases (about one-half the extent of those in the small pupil).

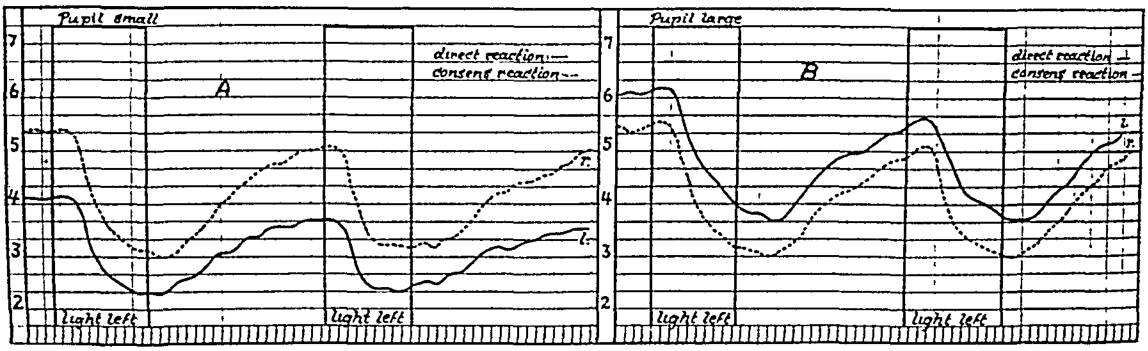

Fig. 6.—Reaction to light of the left pupil in large and small phases.

The solid line represents the directly reacting pupil; the dotted line, the consensually reacting one. *A*, small phase. The primary phase of contraction is normal; the secondary phase is decreased in extent but not in duration, and the tertiary phase is absent. These features are most pronounced in the second light reaction. *B*, large phase. The primary phase of contraction is normal; the secondary phase is more extensive and the tertiary phase is more extensive and longer lasting than in the corresponding phases shown in *A*.

The light reactions of the right pupil (both direct and consensual) were almost the same whether the left pupil was small or large. They were diminished in all phases by cocaine.

C. With Physostigmine.—Physostigmine diminished all light reactions of the left pupil.

1. Small Phase of Left Pupil: The primary phase of contraction was particularly diminished, the reaction becoming very slight and rather sluggish.

2. Large Phase of Left Pupil: Only the primary phase persisted; the secondary and tertiary phases were almost completely abolished.

IV. FATIGUE PHENOMENA

We have already emphasized that all the reactions in this case showed the features of fatigue from the beginning. They further showed increased fatigability to a series of light stimuli.

Reaction to Light of Left Pupil	Extent of Reaction of Left Pupil When Large, Mm.	Extent of Reaction of Left Pupil When Small, Mm.
First	2.47	1.5
Second	1.6	1.37
Third	1.47	1.23
Fourth	1.37	0.97
After psychosensory restitution		
Fifth	2.27	1.33

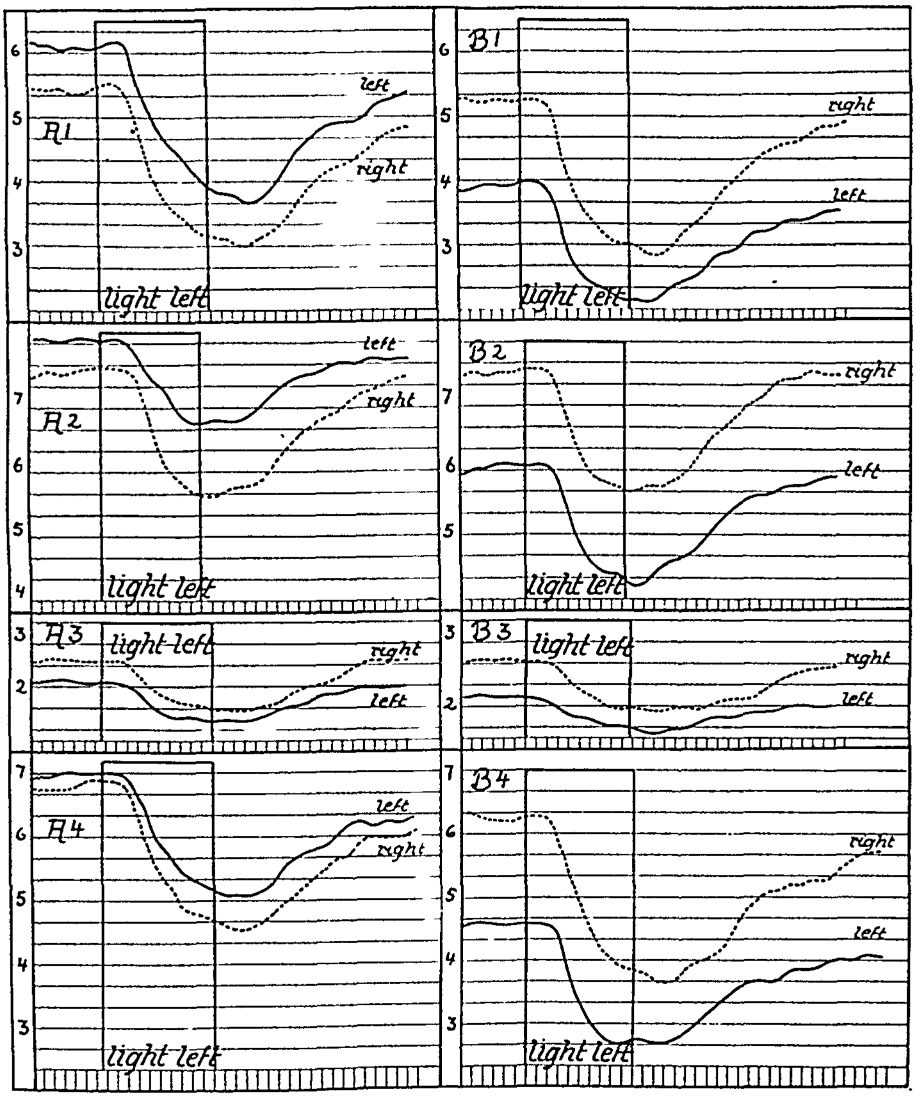

Fig. 7.—First line graphs: Without drugs. *A1,* when the left pupil is large. *B1,* when the left pupil is small.

Second line graphs: After instillation of cocaine. *A2,* when the left pupil is large. The reaction of the left pupil becomes slower and less extensive in all its phases. The static anisocoria increases during contraction (pseudo-oculomotor phenomenon). *B2,* when the left pupil is small. The primary reaction phase is not altered. The secondary and tertiary phases are more rapid and more extensive.

Third line graphs: After instillation of physostigmine. All reactions are diminished. *A3,* when the left pupil is large. The primary phase of contraction persists. The secondary and tertiary phases are almost completely abolished. *B3,* when the left pupil is small. The primary phase of contraction is diminished.

Fourth line graphs: After instillation of epinephrine. The slight change in pupillary reactions is more apparent in the large phase. It somewhat resembles the effect of cocaine.

As shown in this tabulation, the fatigue phenomena occurred much more readily when the left pupil was large than when it was small. The psychosensory

restitution phenomenon, however, was much more effective when the left pupil was large.

It is noteworthy that, in the course of the development of fatigue, tonohaptic reactions [5] sometimes appeared in the left pupil when it was small. The fatigue phenomena affected particularly the secondary and tertiary phases, both of them disappearing almost completely; this greatly diminished the time of contraction, which appeared limited to the primary phase of contraction. This phenomenon affected the left pupil when it was large to a lesser degree, although actually in the same manner. The left pupil showed the same kind of response in both the large and the small stage whether it reacted directly or consensually.

The directly reacting right pupil showed an equally increased fatigability.

V. REACTION TO PSYCHOSENSORY STIMULI

The right pupil reacted to sound to approximately the normal extent. After a latent period, a slow primary phase of dilation set in and was followed by a secondary rapid phase of dilation and a slow phase of recontraction (fig. 8).

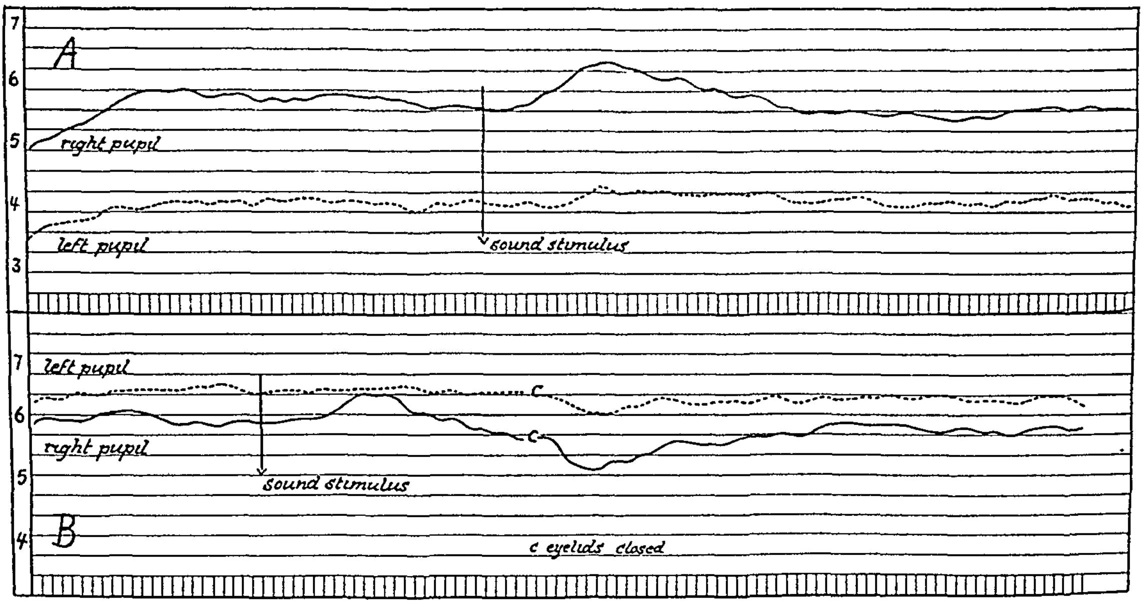

Fig. 8.—Influence of auditory stimulation.

A, small phase of left pupil. The reaction to auditory stimulation is present, but is diminished as compared with that of the right pupil. *B*, large phase of left pupil. There is no reaction on auditory stimulation. At *c* the course of the pupillary curve is interrupted by a lid closure reflex, more extensive on the right side than on the left.

1. The left pupil when small showed a pathologic reaction to sound stimuli; i. e., after an abnormally long latent period, decreased dilation appeared.
2. The left pupil when large was not observed to react to sound stimuli at all.

It is worth noting that in a case of cyclic oculomotor phenomenon,[1] psychosensory dilation was present but was diminished in both the spastic and the paralytic pupillary phase.

VI. PSYCHOSENSORY RESTITUTION PHENOMENON

As previously mentioned, a psychosensory restitution phenomenon existed both when the left pupil was large and when it was small. It was present to a greater degree in the large phase.

5. Lowenstein, O., and Friedman, E. D.: Present State of Pupillography: Its Method and Diagnostic Significance, Arch. Ophth. **27**:969-993 (May) 1942.

When the psychodilation and the spontaneous dilation phase of the left pupil coincided, the light reaction of the left pupil seemed diminished, so that the restitution phenomenon was apparently suppressed. On the other hand, when restitution was attempted during the contraction phase of the left pupil, the effect of the restitution phenomenon seemed to be increased (fig. 9).

VII. INFLUENCE OF DRUGS ON THE PUPILLARY DIAMETER

A. Cocaine.—Under the influence of cocaine, the normal pupil first contracted for a period of 5 to 7 minutes, or even more. This initial contraction was followed by the dilation proper.

The pupillary movements were measured after the instillation of 3 drops of 1 per cent cocaine hydrochloride (second drop three minutes after the first one, and the third drop seven minutes after the first one) both while the left pupil

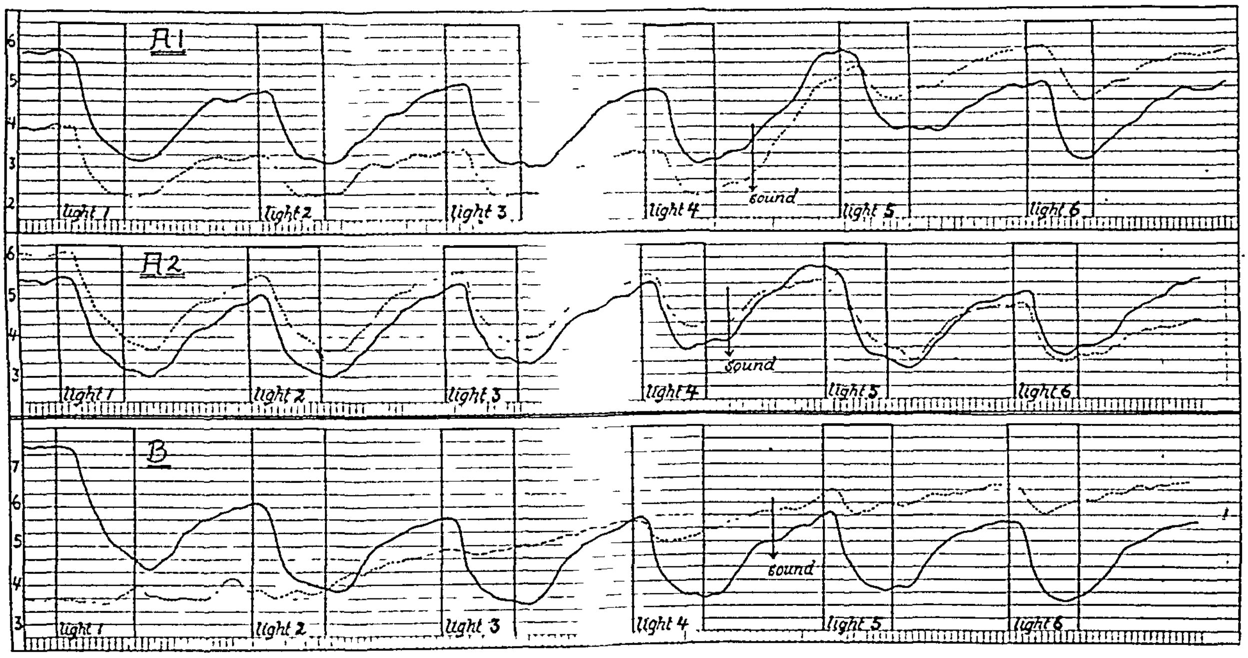

Fig. 9.—Comparison of reactions to light in the case of periodic sympathetic spasm and in a previously reported case of periodic parasympathetic spasm.

A, from the case of sympathetic spasm. *1,* small phase of left pupil. Four reactions to light, showing tendency to tonohaptic responses. A sound produced before the fifth light stimulus coincided with the spontaneous dilation of the left pupil, with production of a dilation of much greater speed than when the sound stimulus was not present. The psychosensory restitution phenomenon was absent as long as active dilation was going on (fifth reaction) but appeared as soon as the active dilation was completed (sixth reaction). *2,* large phase of left pupil. Four reactions to light, showing increased fatigability. Although the pupil was of about the same diameter at the beginning of the fourth reaction as at the beginning of the second, the contraction had been decreased to about two thirds of its earlier value. The auditory stimulus after the fourth reaction to light coincides with the contraction period of the left pupil. The fifth reaction to light is much more extensive than the fourth (about twice). *B,* from the case of cyclic spasm of the third cranial nerve. Contrary to what was found to be the case represented in *A1,* the case of cyclic sympathetic spasm, the sound stimulus did not cause an increase in the speed of the spontaneous pupillary dilation. In this case the psychosensory restitution phenomenon was practically absent in both the small and the large phase of the pupil.

was small and while it was large (fig. 10 *A1* and *B1*). In both stages the pupils showed reactions.

Phase of Left Pupil	Instillation of Cocaine in Both Conjunctival Sacs	Preliminary Contraction, Mm.	Dilation, Mm.
Small	Left pupil	1.0	2.1
	Right pupil	0.9	1.7
Large	Left pupil	0.35	1.45
	Right pupil	0.6	1.5

The significance of the results is as follows: The left pupil reacted to cocaine better in the preliminary and in the dilation phase when the pupil was small than when it was large. The right pupil showed the same feature to a lesser degree.

B. Physostigmine.—As in the normal pupil, the contraction of the pupil was preceded by a slight dilation. Both pupils reacted to physostigmine.

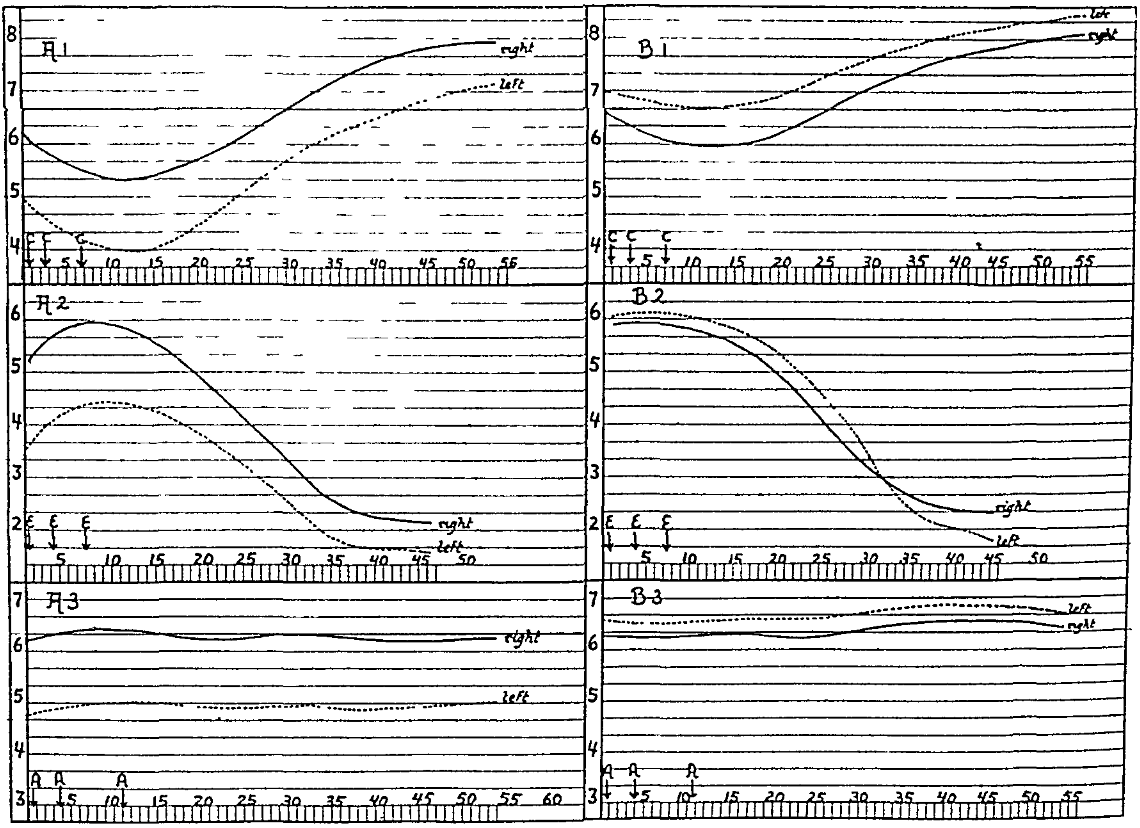

Fig. 10.—Influence of drugs on the size of both pupils during (*A*) the phase of dilation and (*B*) the phase of contraction of the left pupil. Arrows mark the time of instillation of the drug into the conjunctival sac.

First line graphs: Influence of cocaine, when the left pupil is small (*A1*) and when the left pupil is large (*B1*). In both cases, both the right and the left pupil dilate after an initial phase of contraction.

Second line graphs: Influence of physostigmine, when the left pupil is small (*A2*) and when the left pupil is large (*B2*). In both cases both the right and the left pupil contract after an initial phase of dilation.

Third line graphs: Influence of epinephrine, when the left pupil is small (*A3*) and when the left pupil is large (*B3*). There is no noticeable effect on the pupillary diameter.

Phase of Left Pupil	Instillation of Physostigmine in Both Conjunctival Sacs	Preliminary Dilatation. Mm.	Contraction, Mm.
Small	Left pupil	0.9	1.9
	Right pupil	0.8	3.0
Large	Left pupil	0.0-0.1	4.2
	Right pupil	0.0-0.1	3.6

The significance of these results is as follows: The left pupil reacted less to physostigmine in the contraction phase when the pupil was small than when it was large. The reverse was true for the phase of preliminary dilation to physostigmine.

The right pupil behaved similarly both to physostigmine and to cocaine, but to a lesser degree. This indicates that the right pupil was hypersensitive to cocaine and less sensitive to physostigmine when the left pupil was small. It was less sensitive to cocaine and more sensitive to physostigmine when the left pupil was large.

C. Epinephrine.—This drug had no influence at all on the pupils when the left pupil was in its small phase and no clearcut influence when the pupil was in its large phase. (Perhaps it caused a transitory dilatation of 0.33 mm. on the right side and of 0.2 mm. on the left side.)

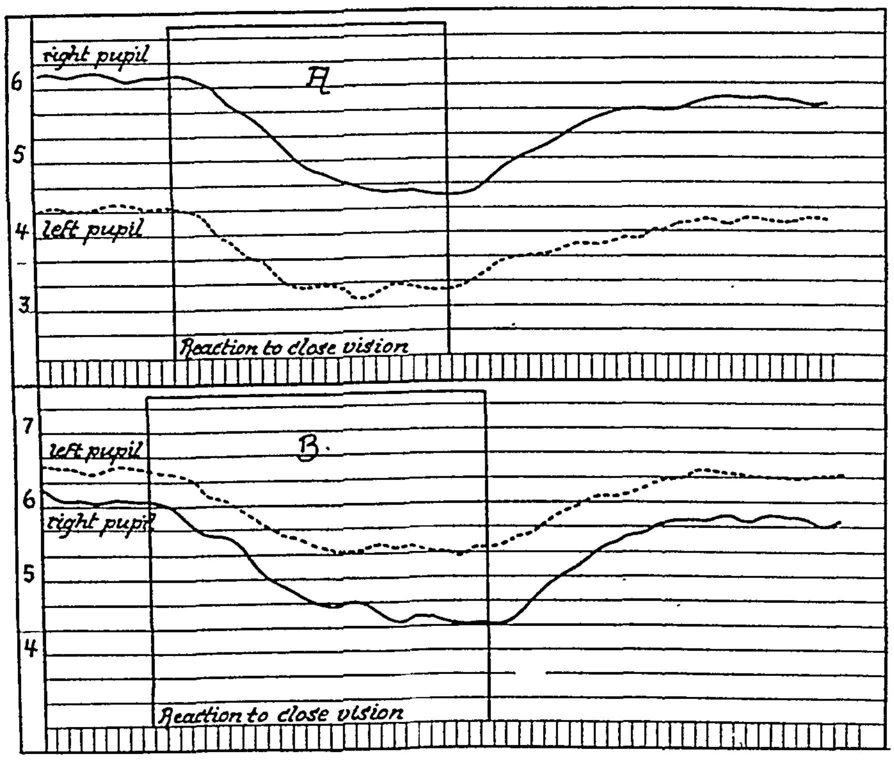

Fig. 11.—Reactions to near and far vision.

A, small phase, and, *B*, large phase, of left pupil. Note that the reactions to near vision are about equal in extent whether the left pupil is small or large. However, when the left pupil is large, contraction seems more sluggish and redilation is more prompt when the pupil is large than when it is small. Anisocoria decreases during redilation when the left pupil is large and increases when it is small. Anisocoria increases during contraction, however, when the left pupil is large and decreases when it is small.

VIII. REFLEXES TO CLOSURE OF LIDS (FIG. 2)

The reaction to closure of the lids, i. e., the contraction and redilation of the pupil following each full or partial closure of the lids, was well developed when the left pupil was in its small phase. In this phase it amounted to approximately 0.8 mm.

When the pupil was large, it was reduced to about one third of its former extent.

IX. REACTION TO NEAR AND FAR VISION (FIG. 11)

A. Large Phase of Left Pupil.—The contraction to near vision amounted to approximately 2 mm. in the left pupil and approximately 2.3 mm. in the right

pupil. The reaction to near vision in the left pupil increased when the convergence movement coincided with the phase of contraction of the left pupil. In that case, the relation of the contraction of the left pupil to that of the right pupil may be 2.16:2.5.

B. Small Phase of Left Pupil.—The contraction of the left pupil amounted to 1.1 mm., and that of the right pupil, to 1.6 mm.

In both phases anisocoria developed, a divergent type (pseudo-oculomotor phenomenon) being present when the left pupil was large and a convergent type when the left pupil was small.

COMMENT

In view of the results of the pupillographic study, three questions are to be discussed: 1. Is one dealing with a sympathetic spasm traveling over the peripheral sympathetic pathways, thereby actively producing dilation of the pupil, or with a periodic inhibition of the parasympathetic nucleus, with passive production of pupillary dilation by relaxation of the nucleus of the third nerve?

2. Where can the lesion be localized?

3. What conclusions can be drawn as to the role played by the peripheral sympathetic innervation in the pupillary movements in man?

1. *Periodic Sympathetic Spasm Versus Periodic Central Inhibition of Parasympathetic Innervation.*—In an earlier publication, one of us (O. L.), in collaboration with Dr. Isidore Givner,[1] discussed the reasons that, in a case of periodic spasm of the third nerve, we could be sure that the disordered function was indeed due to a spasm produced by the nucleus of that nerve. One of the most important considerations was that synchronously with the contraction of the pupil the ipsilateral levator palpebrae muscle would become activated. In the case now in question, a completely analogous situation was observed in the sympathetically controlled opening of the palpebral fissure, as shown in figure 12. A close relation was seen between the dilation of the pupil and the opening of the palpebral fissure. Whether or not a simultaneous periodic exophthalmos existed or whether intraocular pressure increased or decreased in parallel fashion could not be determined with the technical facilities at our disposal. All sympathetic symptoms other than the opening of the palpebral fissure—in particular, differences in temperature between the right and the left side, loss or diminution of axon reflexes on the left side and the results of mecholyl chloride tests—showed constant (and not periodically developing) functional disturbances.

There was only one periodic phenomenon associated with the periodic sympathetic ocular phenomena, that is, the extension spasm of the wrist and the flexion spasm of the third, fourth and fifth fingers of the left hand; since these spasms appeared each time before the ocular symptoms, which never occurred without being preceded by the movements of the hand, they may be considered to be the stimulus exciting the sympathetic ocular reactions.

The periodic widening of the palpebral fissure is in itself strong evidence for the sympathetic origin of the syndrome, for if it were based on a spasm of the third nerve, one would expect simultaneous pupillary contraction, not the pupillary dilation noted in this case. However, there is other evidence for the spastic sympathetic nature of the phenomenon.

We should first mention that the dilation of the pupil is relatively rapid as compared with the reconstriction, which is very slow and takes approximately six times as long as the dilation. By analogy with other reactions, we may assume that active stimulation produces more rapid effects than relaxation. This statement is not contrary to Sherrington's law that each relaxation of the agonists

produces stimulation of the antagonists. It was seen, for instance, in the case of periodic spasm and relaxation of the third nerve reported by Lowenstein and Givner [1] that the contraction was carried on at almost twice the rate of the relaxation (which produced dilation). If the speed of dilation produced by relaxation of the third nerve is compared with the speed of pupillary dilation in this case, it is found that the average speed of the former was much less (0.33 mm. per second) than that in this case (0.4 mm. per second). On the other hand, the speed of recontraction in our case was 0.07 mm. per second; in the case of active contraction within the oculomotor cycle, however, it was 0.93 mm. per second.

When, in the case of periodic spasm of the third nerve light reflexes were elicited while the automatic dilation was in progress, the speed of this dilation could be decreased to 0.15 mm. per second, i. e., to less than one-half the original

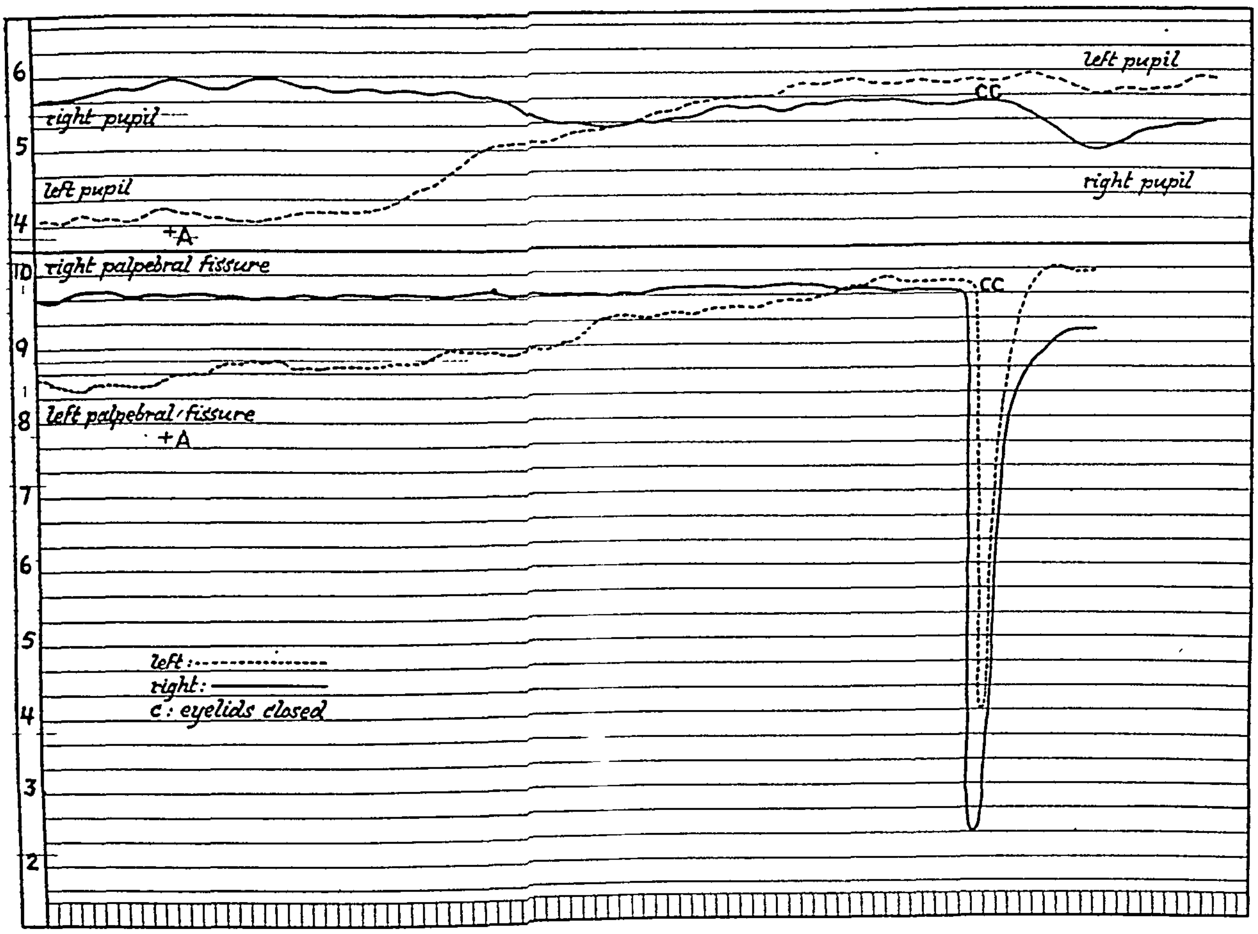

Fig. 12.—Relation of the palpebral fissure to spontaneous movements of the left pupil. When the left pupil becomes large (*A*), a simultaneous enlargement of the left palpebral fissure takes place. Point *cc* indicates the relation of lid closure to the associated pupillary response. The left palpebral fissure was not as completely closed as the right. Likewise, the pupillary contraction on the right side produced by lid closure was more prompt and extensive than that on the left side, while the left pupil was large.

speed; in the present case, however, light reflexes elicited during the phase of dilation of the pupil had no detectable influence on the speed of dilation. Conversely, in the case of oculomotor spasm psychosensory stimulation could not modify the automatic dilation; in the present case, however, such stimulation considerably increased the speed of the dilation. These differences, difficult as they may be to explain in all their details, indicate, nevertheless, that the two processes are undoubtedly different in the 2 cases.

The spastic dilation increased under the influence of cocaine and decreased under the influence of physostigmine. When the left pupil was small, it was

hypersensitive to cocaine and hyposensitive to physostigmine; when large, it was hyposensitive to cocaine and hypersensitive to physostigmine. This fact, too, suggests a sympathetic spasm as the cause of the pupillary dilation.

In line with this argument is the fact that the lid closure reflex, a parasympathetic reflex consisting of pupillary contraction following closure of the lids, was also inhibited during the phase of dilation.

The reaction to near vision caused the disappearance, or at least the diminution, of the anisocoria existing when the pupil was small. This anisocoria, however, was increased at the peak of the contraction when the left pupil was large before the reaction to near vision. This is a phenomenon observed in all cases in which cocaine has caused asymmetric enlargement of the pupil because of decreased sensitivity of one pupil to cocaine. This phenomenon occurs in sympathetic conditions. It is called the pseudo-oculomotor phenomenon (Lowenstein and Franceschetti). The same phenomenon was present in the reactions to light during the periodic phases of active contraction and dilation. It is noteworthy that epinephrine and cocaine produce the phenomenon in the same way.

The psychosensory restitution phenomenon was present to a greater degree in the phase of dilation than in the phase of contraction in the left pupil. This corresponds to the increase in this phenomenon under the influence of cocaine in normal persons, due to increased sensitivity to the liberated epinephrine.

All these facts point to the explanation that the periodic dilation of the pupil is due to an increase in the action of the sympathetic innervation.

2. *Localization of the Lesion.*—The question where the sympathetic system was involved in this case cannot be answered unequivocally. It is probable, however, that the lesion was localized within the first sympathetic neuron, central to the center of Budge.

According to experiments on cats conducted by Hess [5a] and others, a zone for production of mydriasis exists in the posterior hypothalamus and in the region of transition to the midbrain, in an area somewhat lateral to the median line. By stimulation of this region, Hess frequently, although not always, saw simultaneously with pupillary dilation the production of motor symptoms in the lid, bulbus oculi, head and extremities. Since these motor effects were not always, but only frequently, accompanied by the pupillary dilation. Hess assumed that the pupillary reaction was a neighborhood symptom. We therefore suspect that the point of stimulation responsible for the sympathetic phenomenon in the present case was located in the posterior left lateral portion of the hypothalamus, close to the nucleus of the first neuron.

In order to make possible more precise localization of interruptions in the three sympathetic neurons, Foerster and Gagel [6] devised the following scheme:

Drug	Effect on Pupil of Interruption of		
	Third Neuron	Second Neuron	First Neuron
Atropine	+	+	+
Cocaine	—	—	++
Epinephrine	+++	—	—
Pain stimulus	±	±	++

In the present case it may be difficult to make a differential diagnosis on the basis of this scheme because the results obtained when the pupil was considered

5a. Hess, W. R.: Pupille und Zwischenhirn, Klin. Monatsbl. f. Augenh. **103**:407-413, 1939.

6. Foerster, O., and Gagel, O.: Die Vorderseitenstrangdurchschneidung beim Menschen, Ztschr. f. d. ges. Neurol. u. Psychiat. **138**:1-92, 1932.

in its large phase differed from those when it was studied in its small phase. We obtained the following results:

Stimulus	Small Pupil	Large Pupil
Atropine	+	+
Cocaine	++	+
Epinephrine	—	—
Pain stimulus	+	—

In the case of the small pupil one would be entitled to localize the lesion in the first neuron, but what about the large pupil, the characteristics of which are not in accordance with the scheme as given?

Foerster's scheme is concerned with interruptions at the different levels of the sympathetic pathways. In the present case, however, the interruptions were certainly not complete, for it was quite evident that the sympathetic innervation was active, although to a lesser degree, when the pupil was small and, to a greater degree, when the pupil was large.

One of us (Lowenstein), on the basis of pupillographic experience with patients and the results of animal experimentation, has endeavored to construct a scheme by which one may distinguish between sympathetic lesions which are irritative, on the one hand, and those which are paretic and paralytic, on the other. This scheme, to be published in full in a later article, is presented here as it applies to sympathetic disturbances, with particular reference to the present case.

	First Neuron		Present Case	
	Irritative	Paretic	Large Pupil	Small Pupil
Atropine	+	+	+	+
Cocaine	+	+	++	++
Epinephrine	—	—	—	—
Sensory stimuli	±	++	—	+
Light reflex	Tonohaptic; pupillotonic absence of reflex	Tonohaptic; complete or incomplete dilation block	Decreased	Tonohaptic
Psychosensory restitution phenomenon	—	++	±	±
Physostigmine	++	++	++	++
Dynamic anisocoria	—	—	—	—
Pseudo-oculomotor phenomenon	+	+	+	+
Near vision	+	+	+	+

If we base the differential diagnosis in our case on this scheme, we find that the small pupil corresponds to a paretic condition of the central sympathetic innervation. The large stage, however, corresponds to an irritative condition of the central sympathetic system. Neither condition is quite pure; the nucleus of the third nerve, too, may be involved. The state of the psychosensory restitution phenomenon indicates the possibility of a lesion in the communications between the hypothalamus and the nucleus of the third nerve (inhibition pathways of the third nerve).

3. *Role of the Sympathetic Innervation in the Pupillary Movements in Man.*—Since the absence or diminution of the psychosensory restitution phenomenon (while the psychosensory dilation phenomenon was present) indicates interruption or lesion of those pathways by which inhibition and desinhibition of the third nerve goes on, we are able to draw conclusions as to the importance of the sympathetic pathways in pupillary control.

Contrary to the opinions expressed in a number of older and recent publications, we found that in the present case, in which the inhibition pathways to the

nucleus of the third nerve were thought to be poor, the sympathetic system stimulated from a point above the center of Budge produced dilation of the pupil consisting of several phases and resulting in total dilation of about 2.05 mm. in about 5.25 seconds, i. e., with an average speed of about 0.4 mm. per second. The reconstriction occurred in about 30 seconds, with an average speed of about 0.07 mm. per second.

When a light reflex was elicited in this case during the phase of active dilation, the contraction resulting was less than that in either the small stage or the stage of complete dilation. The same was true for other parasympathetic reflexes, for instance, the lid closure reflex. On the other hand, if the parasympathetic reflexes, such as the light or the lid closure reflex, were elicited during the period of active contraction following the spastic dilation, these reflexes were increased and were better developed than they were when the pupil was at the peak of dilation or in the corresponding stage of active dilation (i. e., when its diameter was the same) or after its contraction was complete. These facts give evidence for the conclusion, since active dilation inhibits parasympathetic reflexes and relaxation from dilation enhances them, that a real antagonism exists between the sympathetic and the parasympathetic innervation of the pupil.

When a sound stimulus was given during the active phase of dilation, and the patient was startled, a psychosensory dilation effect was added to the spontaneous dilation. When, however, the same was done in the beginning of the period of relaxation, no psychosensory dilation phenomenon could be observed. This means that in the beginning of the period of relaxation (immediately after complete dilation from sympathetic spasm) the sympathetic nerves were apparently paralyzed to some xetent.

The maximal light reaction was obtained during the large phase—not when the dilation had reached its peak but shortly after the peak had been passed. This means, as has been confirmed by other experiments, that a certain well defined degree of sympathetic innervation is necessary in order to permit a maximal light reaction.

Spastic dilation in itself does not produce the so-called spastic mydriatic pupillary immobility, which was not seen in our case. A certain duration, as well as a sufficiently high degree, of spastic dilation is necessary to production of that phenomenon, as in Adie's pupillary syndrome, in which the spastic mydriatic immobility to light may be suppressed by application of physostigmine (Lowenstein)

The light reflex elicited when the sympathetic innervation is in spastic activity and the reflex elicited when it is relaxed show characteristic differences. When the sympathetic innervation is relaxed and the pupil is small, the primary phase of contraction is present, the secondary phase is diminished and the tertiary phase is absent. When the sympathetic innervation is in spastic activity and the pupil is large, the primary phase of contraction is the same as that in the small pupil, but the secondary and tertiary phases are prolonged. This implies that the sympathetic innervation does not influence the entire contraction to light but affects only the secondary and tertiary phases. If the sympathetic innervation is weakened, a decrease in the secondary and tertiary phases of contraction is therefore produced. When these phases of contraction disappear completely, the so-called tonohaptic type of light reaction appears (Lowenstein and Westphal [7]),

7. Lowenstein, O., and Westphal, A.: Experimentelle und klinische Studien zur Physiologie und Pathologie der Pupillenbewegungen mit besonderer Berücksichtigung der Schizophrenie, Berlin, S. Karger, 1933.

which is characteristic of a certain number of disturbances of the central sympathetic system.

Under the influence of cocaine, both spontaneous pupillary phases (small and large) persisted; however, when a light reaction was elicited in the small phase of the cocainized pupil, this contraction showed, unlike the noncocainized small pupil, a secondary and a tertiary phase of contraction. This means that cocaine activates the secondary and tertiary phases of contraction, which is another proof that these phases are of sympathetic origin. In the large phase of the cocainized pupil, all three phases of contraction of the light reflex were diminished. This means that the development of the secondary and tertiary phases is in direct dependence on the functional integrity of the sympathetic innervation. When, however, this functional capacity surpasses a certain level, not only are the secondary and tertiary phases of contraction abolished, but that portion of the contraction controlled by the third nerve is also neutralized, namely, the primary phase. Spastic mydriatic pupillary immobility results, as in Adie's syndrome.

When the pupil was contracted with physostigmine, both stages produced by spontaneous sympathetic activity persisted. The light reaction in the small physostigminized pupil was sluggish, consisting almost solely of a slow primary contraction. Sympathetic activity, as shown in the large pupillary phase, produced an increase in the primary phase of contraction to light but was not sufficient to produce a secondary and a tertiary phase. This means that the primary phase of contraction, which is enhanced by the sympathetic activity, is an expression of activity of the third nerve, facilitated by neutralization of a certain amount of acetylcholine by the epinephrine elaborated by the sympathetic innervation.

Tonohaptic reactions appear as fatigue symptoms more often when the pupil is small than when it is large, an indication that inactivity of the sympathetic innervation facilitates the oncoming symptoms of fatigue. The first symptoms of fatigue within the light reaction were in this case characterized by disappearance of the secondary and tertiary reaction phases. In cases in which the nucleus of the third nerve is damaged, without superimposed lesion of the sympathetic pathways, the first symptoms of fatigue to appear consist of an initial dilation preceding the contraction.

CONCLUSIONS

A syndrome of periodic sympathetic spasm and subsequent relaxation occurred in a woman aged 22. This patient suffered from a progressive degenerative condition of the central nervous system, characterized by gradual development of motor and sensory disturbances, peculiar gait and periodic spastic extension at the wrist and flexion of the ulnar three fingers, which preceded by some seconds the periodic pupillary phenomena. A number of other sympathetic and parasympathetic symptoms were noted.

Impulses traveling over the sympathetic pathways produce a pupillary dilation consisting of several dilation phases at an average speed of 0.4 mm. per second, which in this case was 2 mm., followed by contraction at an average speed of about 0.07 mm. per second.

The light reflex of the pupil, usually considered to be a parasympathetic reflex, contains in its phase of contraction some factors, particularly the secondary and tertiary phases, which are determined by the functional state of the sympathetic system, whereas the primary phase of contraction depends predominantly on the parasympathetic system.

A certain functional sympathetic tonus is necessary in order that a maximal sympathetic reaction, for example, a maximal psychodilation reflex, may be guaranteed.

A certain, well defined degree of sympathetic innervation is necessary for a maximal parasympathetic reaction, such as the light reflex.

When the secondary and tertiary phases in the contraction of the light reflex are poor, cocaine will improve them.

The primary phase of contraction of the light reflex is the expression proper of the influence of the third cranial nerve. When the pupil is contracted with physostigmine and the primary phase of contraction of the light reflex is poor, it can be improved by the occurrence of spontaneous sympathetic spasm, as a result of the neutralization of physostigmine by the liberated epinephrine.

Poor sympathetic innervation facilitates the occurrence of symptoms of fatigue within the pupillary light reflex, characterized by early disappearance of the secondary and tertiary phases of contraction. There exists another type of fatigue, however, due to damage to the nucleus of the third nerve, which is manifested first as an initial dilatation preceding the contraction to light.

Fatigue of the sympathetic type, due to poor sympathetic innervation, frequently appears in the form of tonohaptic reactions, characterized by loss of the secondary and tertiary phases of contraction.

When the pupil becomes small because of poor sympathetic innervation, hypersensitivity to cocaine and hyposensitivity to physostigmine develops. Conversely, when the pupil becomes large under the influence of hyperinnervation by the sympathetic system, hypersensitivity to physostigmine and hyposensitivity to cocaine develop.

Differentiation of the three phases of contraction by analysis of the light reflex makes it possible to eliminate either the parasympathetic or the sympathetic factor, so that their respective strengths may be evaluated.

865 Park Avenue.

Clinical Notes

A VACUUM DEVICE FOR THE EYELIDS

Henry B. Lemere, M.D., Beverly Hills, Calif.

The expression of the meibomian glands by digital pressure or by some form of spatula, while not very painful, is occasionally objected to by the patient. A few weeks ago, in a situation of this kind, I attached the glass portion of a medicine dropper to the tubing of the suction apparatus I use for nasal displacement treatment. I found that passage of the end of the dropper back and forth along the margin of the lids tended to evacuate concretions from both the meibomian glands and the hair follicles.

The degree of vacuum does not have to be regulated. The end of the dropper is so small that the tube usually collapses and no trauma is produced. If the end happens to slip on to the bulbar conjunctiva, one can immediately stop the pressure by pinching firmly the connecting rubber tubing and then slowly and gently release the point.

Experience with this method has shown that occasionally an eye dropper has an end of greater caliber than usual and is then too large. A dropper with a medium or small end is necessary.

I have found this procedure a valuable adjuvant to treatment in practically all my cases of chronic and in some cases of acute conjunctivitis. I instil a drop of 0.5 per cent solution of pontocaine hydrochloride a minute before I use the suction and 2 drops of a 1 : 500 solution of silver nitrate afterward to take care of any floating material resulting from the suction. This weak solution of silver nitrate does not have to be neutralized. This method of treatment, with the use of sulfathiazole in accordance with Thygeson's[1] directions, gives a much happier outlook in cases of conjunctivitis than has previously been possible.

Some chronic inflammations take a long time to clear up. In selected cases I provide the patient with a piece of rubber tubing attached to the dropper, and he himself, by using mouth suction, can daily evacuate the concretions.

1. Thygeson, P.: Sulfonamide Compounds in Treatment of Ocular Infections, Arch. Ophth. **29**:1000 (June) 1943.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

DIABETIC RETINOPATHY

IRVING H. LEOPOLD, M.D., D.Sc.
PHILADELPHIA

Although all ophthalmologists recognize the typical ophthalmoscopic appearance of diabetic retinopathy, first described by Jaeger[1] in 1856, not all are convinced that the fundic picture is specific. There have been many papers in past years that supported each side of the question.[2] Practically all discussions have been based on observations on patients. The facts that diabetic retinopathy is usually associated with retinal arteriosclerosis, hypertension and renal disease and that young persons with diabetes were formerly thought to be free of the retinopathy have led many observers to conclude that diabetic retinopathy is not specific.[3] On the other hand, recent studies have shown that sclerosis of the retinal vessels is not more frequent in diabetic than in nondiabetic patients of a similar age group.[4] Diabetic retinopathy does occur in young persons if observations are made over a sufficiently long time,[5] and this fundic picture does occur in persons free from hypertension, sclerosis of the retinal vessels and renal disease.[6] Attempts have been made to fit all this evidence into one picture and to find a common denominator—one basic pathologic change common to all cases of diabetic retinopathy. This factor should be one that increases in severity with the duration of the disease, for it is well established that the incidence of retinopathy increases with the length of the diabetic state.[7]

HYPERGLYCEMIA

Since hyperglycemia is a metabolic fault in every case of diabetic retinopathy, Elwyn,[8] and recently Duggan,[9] suggested it as the fundamental cause. In doing so, however, they neglected the considerable evidence of Waite and Beetham,[2i] Arruga,[10] Hanum[11] and others, who demonstrated that diabetic retinopathy is most frequent, not in patients with a very high sugar content of the blood but in those with mild hyperglycemia. Duggan[9] suggested that uncontrolled hyperglycemia prior to the administration of insulin was responsible. He expressed the belief that diabetic retinopathy is essentially a capillary disease. The temporary hypoglycemia produced by insulin calls forth epinephrine, with production of arteriolar constriction, which, in turn, is responsible for capillary anoxia, dilatation and increased permeability. Duggan cited cases of other investigators and his own as instances in which improvement occurred with employment of vasodilator drugs.

From the Department of Ophthalmology, Hospital of the University of Pennsylvania.

1. Jaeger, E.: Beiträge zur Pathologie des Auges, Vienna, 1856.

2. (*a*) Friedenwald, J. S.: Symposium on Diabetic Retinitis, Am. J. Ophth. **8**:61, 1925. (*b*) Gradle, H.: Ocular Conditions in Diabetes, ibid. **10**:54, 1927. (*c*) Cohen, M.: The Eye in Diabetes Mellitus, Arch. Ophth. **2**:530 (Nov.) 1929. (*d*) Cammidge, P. J.: Retinitis in Diabetics, Proc. Roy. Soc. Med. (Sect. Ophth.) **23**:24, 1930. (*e*) Dirion, J. K.: Diabetic Retinitis, Arch. Ophth. **9**:829 (May) 1933. (*f*) Wagener, H. P.; Dry, T. J., and Wilder, R. M.: Retinitis in Diabetes, New England J. Med. **211**:1131, 1934. (*g*) Cohen, M.: Lesions of the Fundus in Essential Hypertension and in Arterial and Renal Diseases, Arch. Ophth. **17**:994 (June) 1937. (*h*) Braun, R.: Diabetic Retinitis: A Study of One Hundred and Fifteen Cases, Arch. f. Ophth. **136**:256, 1936; abstracted, Arch. Ophth. **18**: 167 (July) 1937. (*i*) Waite, J. H., and Beetham, W. P.: Visual Mechanism in Diabetes Mellitus, New England J. Med. **212**:367 and 429, 1935. (*j*) Lee, R. H.: The Ocular Fundus in Diabetes Mellitus, Arch. Ophth. **26**:181 (Aug.) 1941. (*k*) Jaeger.[1]

3. Friedenwald.[2a] Gradle.[2b] Cohen.[2c] Cammidge.[2d] Dirion.[2e] Cohen.[2g] Lee[2j]

4. Wagener, Dry and Wilder.[2f] Waite and Beetham.[2i]

5. (*a*) Barkan, H., and Gray, H.: Diabetes and Retinitis, Tr. Am. Ophth. Soc. **35**:80, 1935. (*b*) O'Brien, C. S., and Allen, J. H.: Ocular Changes in Young Diabetic Patients, J. A. M. A. **120**:190 (Sept. 19) 1942.

6. Gresser, E. B.: Studies of Retinopathies: Diabetes Mellitus, Am. J. Ophth. **16**:612, 1933. Wagener, Dry and Wilder.[2f] Waite and Beetham.[2i] Barkan and Gray.[5a]

7. Waite and Beetham.[2i] Barkan and Gray.[5a]

8. Elwyn, H.: Problem of Diabetic Retinitis, Arch Ophth. **25**:139 (Jan.) 1941.

9. Duggan, W. F.: Clinical Vascular Physiology of the Eye, Am. J. Ophth. **26**:354, 1943.

10. Arruga, H.: Ocular Diabetes, Arch. de oftal hispano-am. **33**:356, 1932; abstracted, Arch. Ophth. **9**:286 (Feb.) 1933.

11. Hanum, S.: Diabetic Retinitis, Acta ophth., 1939, supp. 16, p. 3; abstracted, Am. J. Ophth. **22**:804, 1939.

VASCULAR STATUS

Cohen [12] insisted that sclerosis of the retinal vessels, though not always seen ophthalmoscopically, was probably always present histologically and was the cause of the retinopathy. This hypothesis may be correct, but his pathologic evidence was based on too few cases and did not exclude hypertension as a factor. Cohen received considerable support in this belief. Friedenwald [13] classified diabetic retinopathy as a particular type of arteriosclerosis of the retina. It has been shown that as the severity of sclerosis of retinal vessels increased the incidence of diabetic retinopathy rose.[14] These observations favor an arteriosclerotic origin, but it is also known that arteriosclerosis alone rarely produces retinal changes identical with those of diabetes.[15]

In past analyses, sufficient attention has not been paid to the type of sclerosis encountered in the retinal vessels. One must differentiate atherosclerosis, arteriolar sclerosis, Mönckeberg's sclerosis and senile arteriosclerosis [16] before much significance can be attached to the incidence of the sclerosis. It is true that Mönckeberg's type rarely, if ever, occurs in retinal vessels, but the other forms may cause recognizable changes in these vessels.[17] All these types of sclerosis have been loosely referred to as arteriosclerosis.

There is considerable evidence that, of the types of sclerosis, only atherosclerosis is more frequent in the diabetic than in the nondiabetic patient of the same age group.[18] A few investigators are not convinced that even atherosclerosis is more frequent or that there is any cause and effect relation between diabetes mellitus and atherosclerosis.[19] Atherosclerosis of the retinal vascular tree has been pathologically demonstrated to exist, chiefly in the central retinal artery,[17a] and there are no available data to show that atherosclerosis is either more or less frequent in the central retinal artery of the diabetic person. The data of Bridgett [20] indicate that the presence or absence of atherosclerosis elsewhere in the body cannot be used as evidence for or against the existence of atherosclerosis of the central retinal artery.

Duke-Elder [21] stated that involutional arteriosclerosis, which he asserted is synonymous with diffuse atherosclerosis, and which corresponds to the senile arteriosclerosis of Wilder, Joslin and others, is of greater incidence and severity in the fundus of the diabetic person than in that of the nondiabetic person. The majority of data indicate that sclerosis of vessels elsewhere in the body the size and caliber of retinal vessels is not increased in the diabetic patient,[22] and Wagener, Dry and Wilder [2f] and Waite and Beetham [2i] were unable to demonstrate any increase in sclerosis in the retinal vessels of diabetic patients as compared with those of nondiabetic persons of the same age group.

Recently Wagener and associates,[2f] O'Brien and Allen,[23] Gibson and Smith,[24] Ballantyne [25] and Michaelson and Campbell,[26] as well as others, have directed attention to the venous system of the retina as playing a significant role in pathologic changes in the fundus associated with diabetes. Ballantyne [25] expressed the belief that fulness of the retinal veins is one of the earliest changes in the retina in diabetes mellitus. However, he was unable to explain the cause of this fulness. He suggested a slight obstruction of the central retinal vein and, as evidence of this, presented 16 cases of occlusion of the central vein, in 15 of which the condition

12. Cohen.[2c, g]

13. Friedenwald, J. S.: The Pathology of the Eye, New York, The Macmillan Company, 1929.

14. Leopold, I. H.: Ocular Findings in Ten Year Treated Diabetes Mellitus, Arch. Ophth. **27**:422 (Feb.) 1942. Waite and Beetham.[2i]

15. Lee.[2j] Barkan and Gray.[5a]

16. (*a*) Joslin, E. P.; Root, H. F.; White, P., and Marble, A.: Treatment of Diabetes Mellitus, Philadelphia, Lea & Febiger, 1940, p. 423. (*b*) Wilder, R. M.: Clinical Diabetes Mellitus and Hyperinsulinism, Philadelphia, W. B. Saunders Company, 1940, p. 275.

17. (*a*) Friedenwald, H.: The Pathological Changes in the Retinal Blood Vessels in Arteriosclerosis and Hypertension (Doyne Memorial Lecture), Tr. Ophth. Soc. U. Kingdom **50**:452, 1930. (*b*) Ballantyne, A. J.: The Evolution of Retinal Vascular Disease, ibid. **57**:301, 1937.

18. Joslin, Root, White and Marble,[16a] pp. 424-426. Wilder,[16b] pp. 329-333.

19. (*a*) Lavietes, P. H.: Blood Sugar as a Criterion of Therapy: The Use of Insulin and Protamine Insulin in Treatment of Diabetes, in Steele, J. M., and others: Advances in Internal Medicine, New York, Interscience Publishers, Inc., 1942, vol. 1, p. 41. (*b*) Tolstoi, E., in Conferences on Therapy: Management of Diabetic Emergencies; Treatment of Surgical Patients, J. A. M. A. **115**:529 (Aug. 17) 1940.

20. Bridgett, C. R.: Sclerosis of the Central Artery of Retina, Am. J. Ophth. **9**:725, 1926.

21. Duke-Elder, S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, p. 2732.

22. Joslin, Root, White and Marble,[16a] p. 424. Wilder,[16b] pp. 329-330.

23. O'Brien, C. S., and Allen, J. H.: Unusual Changes in Retinal Veins in Diabetes, Tr. Sect. Ophth., A. M. A., *1940*, p. 148.

24. Gibson, G. G., and Smith, L. W.: Retinal Phlebosclerosis, Tr. Sect. Ophth., A. M. A., *1941*, p. 58.

25. Ballantyne, A. J.: Recent Work on Vascular Disease and Its Significance in Medical Ophthalmology, Glasgow M. J. **138**:1, 1942.

26. Michaelson, I. C., and Campbell, A. C. P.: Anatomy of the Finer Retinal Vessels and Some Observations on Their Significance in Certain Retinal Diseases, Tr. Ophth. Soc. U. Kingdom **60**:71, 1940.

was associated with diabetes. Michaelson and Campbell,[26] working with carefully prepared retinal tissue, indicated that the deep retinal capillary plexus is more closely knit than the superficial capillary plexus, and they therefore concluded that the circulation tends to be relatively more sluggish here, even under normal conditions. These authors noticed in retinal tissue of diabetic patients dilatation of the veins of the third order of division. This dilatation would produce congestion, which would be felt in the capillary system. Since the deep plexus is more dependent than the superficial plexus, the meshwork closer and the circulation slower, the back pressure is more felt there, and blood passes from these vessels into the outer molecular layer, with production of punctate hemorrhages. This theory is a plausible one. However, these observers failed to state the number of cases in which such a pathologic state was observed. Others, namely, Mylius,[27] Elwyn [8] and Ricker,[28] have postulated a similar theory.

Agatston,[29] in a careful pathologic study now under way, noted sclerotic lesions of the veins, which extended to involve the venules and the capillaries. He noted fibrosis of the retinal vessels, hyalinization of the walls and separation of the longitudinally directed fibrils. These changes, although also present in the retina of nonhypertensive and hypertensive patients, were more frequent and severe in diabetic patients. He observed that the capillaries in the internal nuclear layer were most involved. It remains to be seen whether such changes are to be seen in all persons with diabetic retinopathy. Beauvieux and Pesme [30] reported sclerosis and hyalinization of venous walls, while Gibson and Smith [24] noted sclerotic changes in the veins in only 2 of 8 patients with diabetic retinopathy on pathologic examination.

O'Brien and Allen [23] and Gibson and Smith [24] gave good descriptions of venous changes in diabetic persons but were careful to note that such lesions were not always present. The incidence of varices of the retinal veins, for example, in patients with diabetic retinopathy is about 1 per cent. Wagener,[31] who had had wide experience with persons with diabetes mellitus, expressed the opinion that venous changes in the retina are not sufficiently severe or characteristic to account for the changes in diabetic retinopathy, although earlier he had postulated such a theory.[2f]

STATUS OF VITAMIN THERAPY

Friedenwald [32] reported that patients with diabetic retinopathy showed an increased capillary fragility, as indicated by petechial hemorrhages in the skin after standard suction was applied. He claimed that the fragility returned to normal when ascorbic acid and vitamin B complex were given. Later investigators, including Friedenwald himself, failed to confirm these results. However, Yudkin [33] reported benefit from the use of 4 or 5 ounces (120 or 150 cc.) of lemon juice daily, particularly when the pulp was included. Rusznyák and Szent-Györgyi [34] and others [35] expressed the belief that citrin, or vitamin P, is the antifragility factor and that this factor, present in fruit juices, pulp and skin, is absent from synthetic vitamin C. Other observers are still not convinced as to its merits. Although Burch [36] reported benefit from the use of vitamin K in cases of hemorrhagic retinitis, it is well known that this vitamin is effective only in cases in which the prothrombin time is increased. It is not likely that the prothrombin time is increased in all cases of diabetic retinopathy, but no evidence is available to justify any conclusion.

It has been shown that vitamin A deficiency can arise in persons with pancreatic dysfunction, especially with prolonged faulty fat metabolism.[37] Carbohydrate metabolism is deranged in persons with vitamin B avitaminosis.[38] Vitamin C reduces the level of the blood sugar in

27. Mylius, C.: Ueber Retinitis Diabetica, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **51**:150, 1936.

28. Ricker, G.: Pathologie als Naturwissenschaft, Berlin, Julius Springer, 1924.

29. Agatston, S. A.: Clinicopathologic Study of Diabetic Retinitis, Arch. Ophth. **24**:252 (Aug.) 1940.

30. Beauvieux and Pesme, P.: Rétinite diabétique, Arch. d'opht. **40**:65, 1923.

31. Wagener, H. P., in discussion on Gibson and Smith.[24]

32. Friedenwald, J., cited by Gifford, S. R.: Ocular Therapeutics, ed. 3, Philadelphia, Lea & Febiger, 1942, p. 85.

33. Yudkin, A. M.: Vitamins in Treatment and Prevention of Ocular Diseases, Arch. Ophth. **19**:366 (March) 1938.

34. Rusznyák, S., and Szent-Györgyi, A.: Vitamin P, Nature, London **140**:426, 1937.

35. Scarborough, H., and Stewart, C. P.: Effect of Hesperidin on Capillary Fragility, Lancet **2**:110, 1938. Ivy, A. C., and Gray, J. S.: Vitamin P and Capillary Fragility, Internat. Abstr. Surg. **69**:4, 1939; in Surg., Gynec. & Obst., July 1939.

36. Burch, E. P.: Treatment of Hemorrhagic Retinitis with Vitamin K, Minnesota Med. **22**:32, 1939.

37. Wirtshafter, Z. T., and Korenberg, M.: Diabetes Mellitus, Baltimore, Williams & Wilkins Company, 1942, p. 62.

38. Williams, R. R.: The Chemistry and Biological Significance of Thiamin, Science **87**:559, 1938.

patients with diabetes mellitus and does not affect the blood sugar in normal persons.[39] However, there has not been sufficient evidence to show that avitaminosis is the root of evil in diabetic retinopathy.

ENDOCRINE GLANDS

Much experimental work has been done to demonstrate the role of the endocrine glands in diabetes mellitus. Reduced sugar tolerance occurs in patients with acromegaly[40] and basophilic adenoma.[41] Diabetic retinopathy may accompany both these pituitary disturbances. It *is known that removal of the anterior lobe of the* pituitary causes a low sugar content of the blood, increased sensitivity to insulin and decreased breakdown of protein.[37] The pancreatic secretion tends to preserve the depots of foodstuffs in various parts of the body, while the pituitary hormone tends to mobilize these depots.[42]

Thyroxin increases the carbohydrate oxidation of the body tissues,[43] while epinephrine can effect mobilization of the sugar in the blood. Lack of adrenal cortical hormone can result in amelioration of pancreatic diabetes in dogs and of diabetes in man[44]; also, an adrenalectomized animal suffers from inability to mobilize fat from the depots and to transport it to the liver.[45] Estrogen reduces the amount of insulin required.[46] At present there is insufficient evidence that any of the endocrine glands play a direct role in causing diabetic retinopathy, although, through their influence on the level of sugar in the blood, fat metabolism and sensitivity to insulin, they may play a role.

CHEMICAL CONSTITUENTS OF THE BLOOD

Waite and Beetham[2i] and Hanum,[11] in studies on the influence of chemical constituents of the blood other than sugar, were unable to attach any importance to urea, uric acid or creatinine. Cammidge[2d] insisted that calcium played a role, but other investigators failed to confirm his observations.[47]

FAT METABOLISM

For years attention has been paid to fat metabolism in diabetes mellitus. It is now known, largely through the work of Stadie,[48] that when fats are burned to limits of the body's capacity, the excess has to be excreted in the urine and that its accumulation in the tissues is favored. Experimentally it has been shown that depancreatized animals maintained on a regulated diet and insulin still show depositions of lipids in their livers.[49] Lecithin,[50] choline,[51] autoclaved pancreas[52] and lipocaic[53] were found effective in preventing deposition of excessive amounts of lipids in the livers of depancreatized dogs. Dragstedt[53] indicated a parallelism between the development of fat in the liver and arteriosclerosis in dogs deprived of lipocaic. It has been pointed out that with fatty infiltration of the liver the diabetic patient may show an increasing tolerance for carbohydrates and present no signs of poor control.[54] So it is possible, and likely, that subendothelial deposition of fat associated with atherosclerosis occurs in all patients with diabetes, whether controlled or not.

39. Pfleger, R., and Scholl, F.: Diabetes und Vitamin C, Wien. Arch. f. inn. Med. **31**:219, 1937.

40. Cushing, H., and Davidoff, L. M.: The Pathological Findings in Four Autopsied Cases of Acromegaly, Monograph 22, Rockefeller Institute for Medical Research, 1927, p. 131.

41. Cushing, H.: Basophil Adenomas of the Pituitary Body and Their Clinical Manifestations, Bull. Johns Hopkins Hosp. **50**:137, 1932.

42. Long, C. N. H., and Lukens, F. D. W.: Observations on Dog Maintained for Five Weeks Without Adrenals or Pancreas, Proc. Soc. Exper. Biol. & Med. **32**:392, 1934.

43. Foster, D. P., and Lowrie, W. L.: Diabetes Mellitus Associated with Hyperthyroidism, Endocrinology **23**:681, 1938.

44. Long, C. N. H.; Katzin, B., and Fry, E. G.: The Adrenal Cortex and Carbohydrate Metabolism, Endocrinology **26**:309, 1940.

45. Barnes, R. H.; Miller, E. J., and Burr, G. O.: The Effect of Adrenalectomy on the Deposition in the Liver of Spectroscopically Active Fatty Acids, J. Biol. Chem. **140**:241, 1941.

46. Spiegelman, A. R.: Influence of Estrogen on Insulin Requirements of the Diabetic, Proc. Soc. Exper. Biol. & Med. **43**:307, 1940.

47. Lawrence, R. D.; Millar, H. R., and Madders, K.: Blood Calcium in Diabetic Retinitis, Brit. M. J. **2**:559, 1930. Quick, A. J.: A Classification of Hemorrhagic Diseases Due to Defects in the Coagulation Mechanism of the Blood, Am. J. M. Sc. **199**:118, 1940. Waite and Beetham.[2i]

48. Stadie, W. C.: Fat Metabolism in Diabetes Mellitus, J. Clin. Investigation **19**:843, 1940.

49. Chaikoff, I. L., and Kaplan, A.: The Blood Lipids in Completely Depancreatized Dogs Maintained with Insulin, J. Biol. Chem. **106**:267, 1934; Liver Lipids in Completely Depancreatized Dogs Maintained with Insulin, ibid. **108**:201, 1935.

50. Hershey, J. M.: Substitution of Lecithin for Raw Pancreas in the Diet of the Depancreatized Dog, Am. J. Physiol. **93**:657, 1930. Hershey, J. M., and Soskin, S.: Substitution of Lecithin for Raw Pancreas in the Diet of the Depancreatized Dog, ibid. **98**:74, 1931.

51. Best, C. H.; Ferguson, G. C., and Hershey, J. M.: Choline and Liver Fat in Diabetic Dogs, J. Physiol. **79**:94, 1933.

52. Kaplan, A., and Chaikoff, I. L.: Effect of Autoclaved Pancreas upon Lipids of Blood and Liver in Depancreatized Dogs Maintained with Insulin, Proc. Soc. Exper. Biol. & Med. **34**:606, 1936.

53. Dragstedt, L. R.: Present Status of Lipocaic, J. A. M. A. **114**:29 (Jan. 6) 1940.

54. Anderson, G. E.: Problem of Retinitis in the Diabetic Patient, Arch. Ophth. **28**:679 (Oct.) 1942.

It may be that the use of lipocaic or some other insulin-free pancreatic extract may prevent this deposition of fats in vessels, as well as in the liver. The clinical status of these lipotropic agents is unsettled at present.[55]

For one to attach any therapeutic importance to lipotropic agents in the control of sclerosis in cases of diabetes, it is necessary to believe that it is atherosclerosis that is increased in incidence in the diabetic patient and that atherosclerosis is initiated by deposition of fat in the vessel walls. The experiments of Aschoff[56] and Leary[57] favor the theory of deposition of fat in vessel walls as the cause of atherosclerosis. The experiments of Duff[58] and others do not.[59] Although it has been shown that the incidence of diabetic retinopathy increases with increasing ophthalmoscopically recognizable sclerosis of retinal vessels,[60] one must remember that there exists no pathologic proof of increase in atherosclerosis of the central retinal artery associated with diabetes mellitus. So it is clear that the value of a lipotropic agent in prevention of diabetic retinopathy is at best largely theoretic and uncertain.

Hyperlipemia, measured by the level of cholesterol, is often elevated in cases of diabetes mellitus. In the majority of such cases the hyperlipemia is based on dehydration and hemoconcentration.[19a] It disappears when glycosuria is controlled, even though the hyperglycemia persists.[61]

Peters[62] studied the small group of cases with persistently high lipid levels of the blood even when glycosuria and fluid balance are controlled, and showed that the hyperlipemia in these cases is probably based on coincidental lesions, and not on the diabetes mellitus itself.

Experimental studies indicate that hypercholesteremia alone is not capable of producing retinal changes, but that when it is combined with local injury deposits of cholesterol in the retina may result.[63] It may well be that once vascular disease, a form of local injury, appears, the surrounding tissues become more susceptible to possible damage from hyperlipemia. Perhaps lipotropic agents may be helpful here.

It is evident that in attempting to treat diabetic retinopathy one must attack several enemies, not knowing which one is doing the real damage, or even that one is cognizant of all the possible culprits.

TREATMENT

Anderson[54] has recently reviewed the subject of fat metabolism in diabetes mellitus and has suggested three major aims for therapy. These aims are accepted by many metabolic clinicians. The patient should receive a high carbohydrate diet in order that mobilization of fat may be kept to a minimum. The patient should receive sufficient protein, on the basis of work which has demonstrated the protective value of animal protein in preventing accumulation of fat in the liver and degeneration of the liver.[64] Since Dragstedt[53] has shown a parallelism between the development of a fatty liver and arteriosclerosis in dogs, protein may also protect the vessels against deposition of lipids. The caloric intake and the blood sugar should be kept at a level which does not permit the patient (if an adult) to gain or lose weight or allow glycosuria to occur. Many clinicians feel it is safer to permit a trace of sugar in the urine than to subject the patient to the dangers of hypoglycemia, such as may result in angina pectoris and occlusion of the coronary arteries in susceptible persons. Lukens[65] suggested that in any case determination of the cholesterol content of the serum two or three times a year will be of some help in recording of the control of fat metabolism. If more knowledge of the endocrine control of fat metabolism is acquired, it should be useful. At present, administration of thyroid is the only obvious means of lowering the cholesterol content of the blood, and this only in certain states and when carried out with due care. One

55. Klein, C.; Saland, G., and Zurrow, H.: Pancreatic Tissue Extract (Insulin-Free) in the Treatment of Peripheral Vascular Disease, Ann. Int. Med. **18**:214, 1943. Wolffe, J.: Pancreatic Extract, Am. J. Surg. **43**:109, 1939.

56. Aschoff, L.: Lectures on Pathology, New York, Paul B. Hoeber, 1924.

57. Leary, T.: Experimental Atherosclerosis in Rabbit Compared with Human (Coronary) Atherosclerosis, Arch. Path. **17**:453 (April) 1934.

58. Duff, G. L.: Experimental Cholesterol Arteriosclerosis and Its Relationship to Human Arteriosclerosis, Arch. Path. **20**:81 (July); 259 (Aug.) 1935.

59. Weiss, S., and Minot, G. R.: Nutrition in Relation to Arteriosclerosis, in Cowdry, E. V.: Arteriosclerosis: A Survey of the Problem, New York, The Macmillan Company, 1933, p. 233. Watson, E. M., and Wharton, M. A.: A Comparison of Various Diets in the Treatment of Diabetes Mellitus, Quart. J. Med. **4**:277, 1935.

60. Waite and Beetham.[21] Leopold.[14]

61. Chaikoff, I. L.; Smyth, F. S., and Gibbs, G. E.: The Blood Lipids of Diabetic Children, J. Clin. Investigation **15**:627, 1936.

62. Peters, J. P., and Man, E. B.: Serum Lipoids in Diabetes, J. Clin. Investigation **14**:579, 1935.

63. Jess, 1925, cited by Friedenwald.[13] Sugita, 1923, cited by Friedenwald.[13]

64. Goldschmidt, S.; Vars, H. M., and Ravdin, I. S.: The Influence of Foodstuffs upon the Susceptibility of the Liver to Injury by Chloroform and the Probable Mechanism of Their Action, J. Clin. Investigation **18**: 277, 1939.

65. Lukens: Personal communication to the author.

must be certain that ample vitamins are included in the diet. In completion of the diet, fluid balance should be well maintained because, as noted, in many cases hyperlipemia really develops on a basis of dehydration.

Since it is known that the presence of hypertension and renal disease unfavorably influences the incidence of diabetic retinopathy,[7] careful attention must be directed to the avoidance of these conditions. A rise in blood pressure tends to produce hemorrhage in already damaged vessels, or may damage vessels, which hyperlipemia may enhance. A fall in blood pressure may induce harmful ischemia in a patient already adjusted to a high blood pressure. In the presence of renal disease, the acid-base balance must be controlled so that no extra burden of excretion is thrown on the kidneys, and elimination by other routes should be aided.

Duke-Elder [66] stressed the importance of control of sepsis, especially in an effort to reduce the incidence of massive retinal hemorrhages. Richardson,[67] in an attempt to evaluate the influence of diabetes on the antibacterial property of blood, showed that the diabetic patients who were in the most unsatisfactory metabolic balance, formed the smallest amount of agglutinin titer against a specific amount of antigen, such as typhoid vaccine. This, also, should impress one with the importance of prevention of infection, as well as control of the diabetes.

66. Duke-Elder,[21] p. 2733.

67. Richardson, R.: Immunity in Diabetes, J. Clin. Investigation **19**:239, 1940.

PROGNOSIS

Bardsley,[68] Folk and Soskin [69] and recently O'Brien and Allen [5b] and Duggan [9] described cases in which benefit was obtained from therapy. Observations on 100 diabetic patients who had been well treated and who had cooperated well in their therapy for over ten years revealed that no great influence on the incidence and course of diabetic retinopathy could be expected from such treatment.[14]

At present, hyperglycemia, excess deposition of fat, vascular sclerosis and changes in the capillaries and, particularly, in the veins are considered probable causative factors in diabetic retinopathy. Disturbances in chemical constituents of the blood, vitamin deficiencies and endocrine disorders must also be reckoned with. Therapy is largely directed against these possibilities, even though usually such a regimen will not promise the patient prevention or regression.

3400 Spruce Street.

68. Bardsley, in Round Table Discussion on Diabetes Mellitus, Tr. Ophth. Soc. U. Kingdom **40**:43, 1920.

69. Folk, M. L., and Soskin, S.: The Fundus Oculi in Diabetes Mellitus, Am. J. Ophth. **8**:432, 1935.

News and Notes

EDITED BY DR. W. L. BENEDICT

SOCIETY NEWS

Pan-American Congress of Ophthalmology.—The Uruguayan committee in charge of the organization of the Second Pan-American Congress of Ophthalmology, which was to be held in Montevideo, Uruguay, in 1943, resolved to postpone this congress until 1944. The exact date will be announced later. The scientific program as it has been published in previous announcements remains unmodified. It is as follows: The first day will be given to a consideration of social ophthalmology, the morning session to cover "Prevention of Blindness in the Americas" and the afternoon session, "The Status of Trachoma in the Americas." The second day will be devoted to research in ophthalmology, eight studies to be selected by the committee on arrangements. The third day will be given to a consideration of glaucoma, the topics to be "The Preglaucomatous State—Its Diagnosis and Treatment," "New Ideas on Glaucoma Derived from Gonioscopy," "Estimation and Mechanism of the Destructive Effects of Ocular Hypertension" and "Surgical Intervention in Glaucoma and How Far Medical Treatment Can Be Continued." The fourth day will be dedicated to a consideration of the surgical therapy of paralytic strabismus, heterophoria and concomitant strabismus, and the fifth day, to free discussion of topics selected by the congressists.

Association for Research in Ophthalmology.—A meeting of the Association for Research in Ophthalmology will be held June 13, 1944 at the Hotel Sherman, Chicago. Applications for places on the program are being received, and all communications should be mailed to the secretary, Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.

UNIVERSITY NEWS

University of Kansas School of Medicine.—Dr. E. J. Curran, Kansas City, Mo., has contributed $10,000 to the University of Kansas School of Medicine for equipment, material and assistance for research in the department of ophthalmology of the medical school.

SPECIAL NEWS

Benjamin Franklin Bifocal Glasses.—The National Franklin Committee, organized by the Franklin Institute, in Philadelphia, in referring to Benjamin Franklin's contributions to medical science, speaks of the discovery of bifocal glasses and quotes the original words:

"Before that year [1784], I had used two pair of spectacles which I shifted occasionally, as in travelling I sometimes read and often wanted to regard the scenery. Finding this change troublesome and not always sufficiently ready, I had the glasses cut and half of each kind (of lens) associated in the same circle."

Correspondence

OPERATIVE TREATMENT OF SQUINT

To the Editor.—I have just read the interesting article by Major H. Saul Sugar in the November 1943 issue of the ARCHIVES which concerns the operative treatment of squint. This study parallels one which I had been carrying on for two years or more at the Brooklyn Eye and Ear Hospital but which, unfortunately, was interrupted by my entry into active military service.

There is one important point which Major Sugar has apparently not touched on, namely, the postoperative interval after which his final determinations on the degree of correction afforded were made. In my own experience, changes have occurred up to six months after operation, and any determination of correction prior to that time should accordingly be considered tentative.

LIEUTENANT COLONEL EDWIN N. BEERY,
Medical Corps, Army of the United States.

96 Remsen Street, Brooklyn.

Obituaries

CHARLES H. MAY, M.D.

1861-1943

In the passing of Dr. Charles H. May, ophthalmology has lost an outstanding figure, a great teacher and a physician of unsurpassed integrity. His death on Dec. 7, 1943, in the eighty-third year of his life, occurred exactly one month after the celebration of his golden wedding anniversary. His life was a long and full one, replete with the satisfactions that came with years of service to his fellow men.

Charles Henry May, the son of Henry May and Henrietta Oppenheimer May, was born in Baltimore on Aug. 7, 1861. Four years later his family moved to New York city, his future home. A brilliant student, young Charles led his class in the private and public schools he attended, as well as at the College of the City of New York. Too young to enter medical school and the career of medicine on which he had set his heart, he entered the College of Pharmacy of the City of New York, graduating at the head of his class in 1879, with the award of a gold medal. He enrolled in Columbia University College of Physicians and Surgeons, graduating with the degree of Doctor of Medicine in June 1883, with the first Harsen Prize for Clinical Reports and the first Harsen Prize for Proficiency at Examination. The title of his graduation thesis was "Statistics of Four Hundred Cases of Rheumatism Treated at the Roosevelt Hospital," a subject suggested by Dr. William H. Draper. Dr. May's brilliant scholastic record led to his nomination, without further examination, to the position of junior assistant to Bellevue Hospital, with the choice of the medical or the surgical side, according to a formal letter from Dr. John G. Curtis, secretary of the faculty of the College of Physicians and Surgeons. The young physician declined this offer, since he had received and accepted an appointment at Mount Sinai Hospital to the medical division, under Dr. E. G. Janeway, Dr. Alfred Meyer and Dr. Rudisch Heinemann.

After leaving Mount Sinai Hospital, he went into private practice, in 1885, with an office on East Fifty-Eighth Street. He worked with Sequin in nervous diseases, Delafield in internal medicine and Agnew in ophthalmology. Dr. May's decision to enter the specialty of diseases of the eye was influenced by the kindness and friendship of Cornelius R. Agnew, professor of ophthalmology at Columbia University College of Physicians and Surgeons.

By 1887 Dr. May had accumulated enough money to go to Europe. He spent six months at Halle, Germany, studying the eye and ear under Alfred Graefe and Hermann Schwartze, and then spent a month visiting the ophthalmic clinics of Berlin. During this period, he met Hermann von Helmholtz and received permission to translate his book on "Physiological Optics." This project failed because no American publisher would undertake to bring out the book.

Six months were spent in the Vienna clinics of E. Fuchs, Dimmer, Koenigstein, Politzer and Urbantschitch. On his way home, Dr. May spent a few weeks in Paris, visiting the clinics of Landolt, Galezowsky, de Wecker and Panas, and in London, at Moorfields.

Returning to the United States in 1888, he opened an office in New York city, on Madison Avenue at Fifty-Ninth Street, later moving to the house he purchased at 698 Madison Avenue. First he practiced both otology and ophthalmology, receiving appointments at the Manhattan Eye and Ear Infirmary, the New York Ophthalmic and Aural Institute and the College of Physicians and Surgeons. Soon after Agnew's death in 1888, Dr. May resigned from the first-named appointment and spent his hours in the clinics at the last two institutions, destined to become the Herman Knapp Memorial Hospital and the Vanderbilt Clinic. He became chief of clinic at the Vanderbilt Clinic after the resignation of Dr. John E. Weeks, holding that position until 1903. Dr. May became associated with the New York Polyclinic Hospital, lecturing in ophthalmoscopy and diseases of the eye from 1886 to 1890. At Mount Sinai Hospital, he was made an assisting attending physician in the department of ophthalmology in 1893, becoming a full attending physician later, when Dr. Gruening retired.

In 1914 he was asked to establish an ophthalmologic service at Bellevue Hospital, where a ward of forty-five beds was equipped according to his plans. He remained as director of this service until 1925, when he resigned, to be succeeded by Dr. John M. Wheeler. Thereafter he was consulting ophthalmologist to Bellevue,

Mount Sinai, French and Monmouth Memorial Hospitals.

His private practice was large, and in his later years he was assisted in his work by young associates, among them Dr. William B. Doherty, Dr. Edward Bassen and, since 1935, a nephew, Dr. Charles A. Perera. Medical visitors from all over the world visited his office, many from among those whom he had taught to use the ophthalmoscope and to recognize diseases of the eyes.

Dr. May often stated that the man who knew more about ophthalmology than any one with whom he was ever associated was Herman Knapp. Dr. May's obituary of Knapp, published in *Ophthalmology* 7:727 [July] 1911, revealed the admiration of a devoted friend and follower for a great teacher.

In 1900 Dr. May devised an improved double disk ophthalmoscope (*Ann. Ophth.* 9:73 [Jan.] 1900), and in 1914 he reported on a new electric ophthalmoscope (*New York M. J.* 100:229 [Aug. 1] 1914), with replacement of the customary fragile mirror by a solid piece of glass, which acts both as a condenser and as a reflector, and the addition of a convex condensing lens immediately above the lamp. This improvement in the electric ophthalmoscope, which William S Dennett had invented in 1885, was given to the medical profession by its inventor and is now in general use.

CHARLES H. MAY, M.D.
1861-1943

In 1893 he married Rosalie Allen, who, together with his two sisters, Mrs. Florence Oppenheimer and Mrs. Nellie Mosbacher, survives him.

He was a member of the American Ophthalmological Society, the American Academy of Ophthalmology and Otolaryngology, the New York Academy of Medicine, the American College of Surgeons, the American Medical Association and the New York State and County Medical Societies.

In the field of medical writing Dr. May was a master. His most widely known work is his

"Manual of the Diseases of the Eye," which has gone through eighteen editions since 1900, the last three revisions having been produced with the assistance of Dr. Charles A. Perera. This book is in wide use as a textbook for medical students and general practitioners of medicine, and it has been translated into many foreign languages, the most recent one being the Portuguese. To Dr. May his textbook was a real child. He read the ophthalmologic literature assiduously, ever seeking to keep his book up-to-date. Just two weeks before his death, he insisted on completing the correction of proof of the eighteenth edition of his brain child.

It is not generally known that Dr. May's first book was "Diseases of Women," published in 1885 by Lea Bros. & Co., Philadelphia. This book was well received and went into a second edition, revised by Leonard S. Rau in 1890. During his early years of practice, Dr. May compiled several textbooks for grammar schools on anatomy, physiology and hygiene, published by William Wood & Co., New York, which went through several editions, the last in 1896. He also wrote, with Dr. Charles F. Mason, an index of materia medica in 1887. He wrote on ophthalmic subjects for the "International Encyclopedia," the "Reference Handbook of the Medical Sciences" and for a number of lay periodicals.

Dr. May was an artist of ability in painting lesions of the fundus and illustrated not only his own writings but those of several colleagues.

He was a skilful surgeon and able therapeutist in his chosen field. He was one of the first in this country to report, in 1899, on the restoration of the conjunctival cul-de-sac in a case of total symblepharon by means of Thiersch skin grafts, and, in 1901, the restoration of a socket by the use of a large Wolff graft. He published papers on the prevention and treatment of ophthalmia neonatorum in 1895, 1906 and 1908.

Physically active until he sustained a fracture of the leg, in an automobile accident in 1910, which delayed in uniting, he was compelled to give up the walks which were one of his relaxations. His main extraprofessional hobbies were limited to visits with his friends, the enjoyment of good cigars, an occasional game of bridge, the reading of detective stories and summer travels in Europe. He crossed the Atlantic every summer for many years, making in all fifty-four trips. He often visited the home of his friend, E. Fuchs, who returned the visits on his trips to this country.

During the World War of 1914-1918 his crippled leg prevented his serving his country in the armed forces. His colleagues in service received from Dr. May, when they returned to their practices, checks for the full fees he had collected from their patients.

As a consultant, he was superb, both in the handling of patients and in arriving at careful diagnoses and decisions. His opinions were of great value because they were based on a complete study of the problem, conservative judgment and vast experience. He was always careful to preserve the reputation of his colleagues and made every effort to have patients return to their former oculists when they came to him for his advice. His ethical standards were so high and his deeds so closely approximated his ideals that he was an inspiring model to watch and follow.

His ability and impartiality were so well recognized that he was employed by governmental agencies, industrial groups, insurance companies and injured workmen to investigate ocular injuries and give an honest verdict. As a special witness in court, he always commanded respect because of his knowledge, experience and integrity. He had a profound disgust for the few colleagues he encountered who perjured themselves in court and took sides without regard to truth and justice.

In handling patients he was without a peer. He knew when to reassure, when to be sympathetic and when to be firm. Patients with a hopeless prognosis were given a feeling of courage by his words.

Like all great men, his kind and generous deeds were hidden. No one who sought his help was turned away.

CHARLES A. PERERA.

Abstracts from Current Literature

Edited by Dr. William Zentmayer

Anatomy and Embryology

Anatomic Factors that Influence the Depth of the Anterior Chamber: Their Significance. H. S. Sugar, Am. J. Ophth. **25:** 1341 (Nov.) 1942.

Sugar draws the following conclusions:

"1. As age advances, the crystalline lens increases in size, thus decreasing the axial depth of the anterior chamber.

"2. The depth of the anterior chamber appears to have a definite relationship to the refractive error of the eye. Myopic eyes tend to have deeper anterior chambers whereas the hyperopic have relatively shallower chambers. This is related to the axial length of the eyeball.

"3. The importance of the anatomic factors in the etiology of acute glaucoma is emphasized. They are significant in making possible measures for the prevention and early detection of this condition."

W. S. Reese.

Congenital Anomalies

Unilateral Melanosis Irides. R. E. R. Mitton, Indian J. Ophth. **4:** 5 (Jan.) 1943.

A Punjabi woman aged 34 had a light golden brown iris in the right eye, while the iris of the left eye was partly golden brown and partly African brown. Biomicroscopic examination showed that the texture of the iris in the melanotic areas differed from that in the lighter areas in that it presented small mamillations. These elevations were close together and entirely confined to the deeply pigmented areas. They seemed superficial, but the deeper stroma was also heavily pigmented.

The pupils dilated unequally, and the pupil of the left eye had a straight upper border; that is, the part of the iris which was pigmented throughout its width underwent less contraction than the part in which the melanin was less evenly distributed. Refraction showed mixed astigmatism.

W. Zentmayer.

Cornea and Sclera

Nodular Keratitis. O. H. Ellis, Am. J. Ophth. **25:** 1224 (Oct.) 1942.

Ellis reports a case of nodular keratitis observed from its incipiency. The patient's mother, 2 aunts, 2 sisters, a niece and probably her paternal great-grandfather all suffered from the condition. Surgical treatment did not improve the vision. Since the condition began with the onset of the menses and the pain ceased during two pregnancies, Ellis feels that it may have been due to an endocrine imbalance.

W. S. Reese.

White Rings in the Cornea (Coats). J. Waldman, Am. J. Ophth. **25:** 1362 (Nov.) 1942.

Waldman concludes that white rings in the cornea (Coats) occur more frequently than the literature indicates, and suggests routine biomicroscopic examination as a means by which their incidence and causation may be learned.

W. S. Reese.

A CASE OF FISTULA OF THE CORNEA: A METHOD OF TREATMENT. J. B. MCAREVEY, Brit. J. Ophth. 27: 306 (July) 1943.

McArevey records a case of traumatic fistula of the cornea in a man aged 27. Fluorescein aided in confirmation of the diagnosis. The diameter of the hole was uniform and measured 1 mm. On the basis of the assumption that with so slight a loss of tissue the swelling of the corneal stroma might close the hole and allow cicatrization to take place if the sides of the fistula were freshened up, a series of perforations were made into the clear portion of the cornea just outside the opacity with a discission needle; these perforations were intended to enter the fistula at different levels. In addition, three small incisions were made into the corneal stroma with a Ziegler knife. A fine probe was passed into these openings, and the corneal tissue was pushed toward the fistula. The anterior chamber had reformed in forty-eight hours.

W. ZENTMAYER.

Glaucoma

AQUEOUS VEINS. K. W. ASCHER, Am. J. Ophth. 25: 1301 (Nov.) 1942.

Ascher finds that appearance of the glass rod phenomenon in aqueous veins is extremely rare in eyes with primary compensated glaucoma as compared with its induction in normal eyes. He discusses the effect of drugs on aqueous veins and stresses the importance of these veins in the understanding of the problems of glaucoma.

W. S. REESE.

Injuries

CHANGES IN THE CILIARY BODY AFTER CONTUSIO BULBI IN WHICH ONLY THE ANTERIOR SEGMENT OF THE EYE IS AFFECTED. G. L. KILGORE, Am. J. Ophth. 25: 1095 (Sept.) 1942.

Kilgore gives the following summary:

"1. Sections of eyes that have suffered experimental contusio bulbi have been presented to show the pathology found in the ciliary body after contusions.

"2. Symptoms following even minor blows to the front of the eye can be explained by the cyclitic changes.

"3. Atrophy of the ciliary body may explain some of the prolonged visual disturbances.

"4. The prognosis should be guarded in cases of contusion. Insignificant blows may be followed by a permanent visual disability.

"5. A case report is submitted to illustrate the practical correlation of pathologic and clinical observations."

W. S. REESE.

"ARC FLASH" CONJUNCTIVITIS, ACTINIC CONJUNCTIVITIS FROM ELECTRIC WELDING ARC. F. E. RIEKE, J. A. M. A. 122: 734 (July 10) 1943.

Rieke considers it unfortunate that the term "arc flash" has been given to ultraviolet conjunctivitis, as it implies that the conjunctivitis is commonly incurred through the incaution or unguarded exposure of the eyes to the flash of the welder's first brilliant contact spark and thus is an instantaneous affair. This can occur, but the injured person must be very close to the arc, within 1 or 2 feet (0.3 or 0.6 meter), and this infrequently happens. It is so usual as to be the rule that the painful eyes of "arc flash" result from an excessive exposure to the arc over a minimum of several minutes, more commonly several hours of time spread through the working shift. It is a cumulative injury, similar in pathogenesis to that of snow blindness and sunburn, which obviously are quantitatively related to the pigmentation of the skin and the length of time spent in the sun's rays.

The author gives the following summary: "Actinic conjunctivitis, or 'arc flash,' as seen in the Oregon Shipbuilding Corporation and the Kaiser Company, Inc., Portland, among 57,000 shipyard workers exposed at various times to the emanations from electric arc welding, is defined as a conjunctivitis caused by excessive exposure to the welder's electric arc and characterized by delayed onset, self-limited course of twenty-four hours, pronounced bulbar hyperemia, swelling of the lids, slight 'sunburn' of the face, absence of discharge other than tears, extreme photophobia and a feeling of sand in the eyes.

"Treatment is given for relief of symptoms through dark glasses, cold applications and the use of local anesthetic, vasoconstricting, mydriatic, lubricating and sedative preparations.

"Prophylactic measures are outlined for the patient and his environment which can completely prevent occurrence of the injury."

W. Zentmayer.

Treatment of Photophthalmia Following Exposure to Rays of Welding Arc. C. E. Benson, U. S. Nav. M. Bull. **41:** 737 (May) 1943.

Benson directs attention to the problem of exposure of the eyes to the radiant energy of the welding arc with the resultant photophthalmia. This type of injury to the eyes, also called actinic ray ophthalmia or "flash," is frequent in shipyards and in plants where welding plays a large part. It is not the welder who is the most frequent victim of his own arc but the workman engaged in work near the welder. The welder protects himself with his hood. He may, however, receive an injury from the actinic rays of the arc of another welder near him or from his own "accidentally struck" arc while his own hood is raised. After exposure to the arc a latent period follows, which may vary from two to fifteen hours. The lesion then manifests itself with sudden onset of intense photophobia, lacrimation and a burning sensation in the eyes. The most frequent complaint is that of a feeling of "sand in the eyes." The lesion is bilateral, although at times the symptoms appear earlier in one eye than in the other; in the present series the majority of "one-eyed flashes" were caused by foreign bodies. The conjunctival vessels are moderately dilated, but this congestion is usually limited to the area of the palpebral fissure. Prevention can be accomplished by protection of the eyes with a shield, hood or goggles. Seventy-three patients were treated with 2 per cent butacaine sulfate and 1 per cent diothane hydrochloride, and 447 patients, with a solution containing 0.25 per cent nupercaine hydrochloride and 0.5 per cent neo-synephrine hydrochloride as the active principles. The nupercaine was used because of its relatively prolonged anesthetic action. Neo-synephrine was added to overcome the vasodilatation and to neutralize partially the contraction of the pupils accompanying many lesions produced by actinic rays. The nupercaine–neo-synephrine solution was dissolved in an aqueous base of zephiran chloride (1:5,000) to decrease the surface tension of the solution, to produce better penetration and to furnish an antiseptic medium. About 2,500 additional patients were treated by the nupercaine–neo-synephrine routine. The treatment did not appreciably decrease the duration of the reparative process. It gave considerable symptomatic relief and helped in the return of men to their work with a minimum of lost time and with no apparent permanent injury.

J. A. M. A. (W. Zentmayer).

Traumatic Oedema of the Macula. S. Philps, Brit. J. Ophth. **27:** 305 (July) 1943.

Philps reports 4 cases of commotio retinae because they represent four stages in the progress of macular edema—edema of the macula, edema replaced by pigmentary changes, hole formation and retinal detachment.

W. Zentmayer.

Instruments

A Modification of Arruga's Speculum. H. Neame, Brit. J. Ophth. 27: 310 (July) 1943.

For operation in cases of detachment of the retina, Arruga's speculum of plated metal was taken as a model, and an instrument made of plastic material was designed 2 mm. wider than the original, so as to give a larger field within the hollow of the retractor for the application of diathermy in treatment of the condition.

The plastic material is roughened for a small area on its convex surface and for a larger area in the hollow of the concave side. Light enters from a small battery or through a transformer from the main at the handle, is carried by internal reflection to the end of the instrument and is dispersed only when it meets the roughened surface. The retractor, of course, is quite free from heat. The illumination of the area of the sclera requiring treatment is admirable and entirely obviates the presence of any shadows. The greater width of the speculum is also an advantage. The third, and definite, advantage of this instrument is that it is a nonconductor of electricity. The article is illustrated. W. Zentmayer.

Operations

A New and Improved Technique for the Closure of Cataract Incisions. C. H. DeVaul, Am. J. Ophth. 25: 1079 (Sept.) 1942.

DeVaul describes a rather involved method for suture of cataract incisions. He first circumsizes the upper two fifths (his illustration appears to show at least three fifths) of the cornea and undermines the conjunctival flap. He then fashions two scleral flaps at the upper limbus and inserts sutures so that the conjunctiva as well as the sclera is closed when these sutures are tied after the extraction. These sutures are then laid aside, and the incision is made as usual, the knife being brought out between the scleral flaps After extraction of the lens the sutures are drawn tight but not tied until reposition of the iris pillars is effected.

W. S. Reese.

Physiology

Gonioscopic Study on the Canal of Schlemm. P. C. Kronfeld, H. I. McGarry and H. E. Smith, Am. J. Ophth. 25: 1163 (Oct.) 1942.

The authors draw the following conclusions from their studies on Schlemm's canal.

"1. Following a sudden lowering of the intraocular pressure induced by aspiration of aqueous or compression of the globe by means of an ophthalmodynamometer, the canal of Schlemm becomes gonioscopically visible in nonglaucomatous eyes, blood taking the place of the usual colorless contents.

"2. Pressure exerted upon the eyeball by the contact lens is not conducive to eliciting this phenomenon but rather to effacing it.

"3. Eyes affected with wide-angle glaucoma show the filling of Schlemm's canal, either in an atypical form or after greater drops in intraocular pressure than are required to induce the phenomenon in nonglaucomatous eyes, or they fail to show it altogether." W. S. Reese.

Some Observations and Experimental Studies on the Physiology of the Ciliary Muscle. E. Sachs, Am. J. Ophth. 25: 1277 (Nov.) 1942.

Sachs gives the following summary:

"1. A backward movement of the anterior coronal region of the ciliary body was demonstrated to be a normal component of the ciliary-muscle contraction in both

dogs and cats. A narrow neutral zone separated this backward-moving region from the forward-moving tissue of the posterior part of the ciliary body and that of the choroid.

"2. The distance of the neutral zone from the limbus varied from 2.0 to 5.0 mm. in 11 dogs, and from 4.0 to 7.0 mm. in 6 cats.

"3. The extent and distribution of the backward and the forward movement (in 11 and 33 eyes, respectively) were measured along a meridian. Some eyes showed a definite peak, while others exhibited a homogeneous distribution of movement.

"4. The contraction time in the dog was about 5 seconds as compared with 3 seconds in the cat (seven and five eyes, respectively).

"5. The force of contraction producing the main (forward) movement in a narrow (about 1.75-mm.) strip of uvea was balanced by a second force, of known magnitude in milligrams. A pull of more than 200 mg. (the maximum recordable by the instrument) was not infrequently found.

"6. No significant difference in force was found between the temporal and nasal sectors.

"7. The elastic resistance offered by a strip of choroid about 1.75 mm. wide to a minimally distortive longitudinal pull was measured in nine eyes and found to be 14.0 to 33.0 mg. in the dog and 14.0 to 24.0 mg. in the cat. Measurements of the resistance in the posterior part of the choroid during stimulation of the ciliary muscle showed no change.

"8. The influence of the intraocular pressure on the contraction of the ciliary muscle was studied in six cat eyes. There was a definite impairment of muscle efficiency at 80 mm. Hg, while no influence could be demonstrated between 11 mm. and 60 mm. Hg.

"9. The significance of these findings is discussed." W. S. Reese.

Refraction and Accommodation

Myopia. A. Cowan, Am. J. Ophth. **25:** 844 (July) 1942.

Cowan disagrees with Donders' statement that because an eye is myopic it must be considered unsound. He cites the conflicting theories of the cause of myopia and its distribution. He insists that myopia is a simple error of refraction and that the terms "pathologic," "malignant" and "pernicious" should be abandoned, as they indicate some disease that either occurs with or happens to result in myopia. He believes in the full correction of myopia and emphasizes the importance of prevention of disease in myopic eyes. W. S. Reese.

Retina and Optic Nerve

Angioid Streaking of the Retina. L. Lehrfeld and S. S. Brav, Am. J. Ophth. **25:** 1222 (Oct.) 1942.

Lehrfeld and Brav report 2 cases of angioid streaks of the retina associated with pseudoxanthoma elasticum in sisters. W. S. Reese.

Chorioretinitis Associated with Positive Serologic Tests for Toxoplasma in Older Children and Adults. D. Vail, J. C. Strong and W. V. Stephenson, Am. J. Ophth. **26:** 133 (Feb.) 1943.

The authors give the following summary:

"Six cases of chorioretinitis of previously unknown etiology are reported in which the presence of positive neutralization antibodies for Toxoplasma was proved. The condition may be either congenital or acquired. The only symptom may be that

of poor or decreasing vision. The fundus usually reveals a chorioretinitic lesion, unilateral or bilateral, having a predilection for the macular area. It has a grayish-white center, is irregular, bordered with dark pigment, and surrounded on one or more sides by faint choroidal hemorrhage. The spread of the lesion is usually in the direction of the hemorrhage. The lesion may be elevated. Iridocyclitis, vitreous opacities, retinitis proliferans, and detachment of the retina may result. Central vision is always adversely affected."

W. S. REESE.

THE DETECTION AND SIGNIFICANCE OF MELANOPHORE EXPANDING SUBSTANCE IN URINE AND BLOOD WITH SPECIAL REFERENCE TO RETINITIS PIGMENTOSA. J. R. MUTCH and D. MACKAY, Brit. J. Ophth. **27**: 434 (Oct.) 1943.

Mutch and Mackay give the following summary:

"The literature on the possible rôle of B-hormone in vision and its relationship to the pathogenesis of retinitis pigmentosa is briefly reviewed, and the techniques for the assay of B-hormone are discussed.

"The results of several urinanalyses for B-hormone are summarised. Reasons are quoted for considering the present assays for B-hormone as not completely specific.

"Experiments are reported in which blood samples from 9 retinitis pigmentosa patients were assayed and compared with blood samples from 7 normal controls. Details are given of the process of extraction and assay employed. Only 3 of the 9 retinitis pigmentosa samples were definitely 'positive.' Two of the 7 control samples gave a positive result.

"It is concluded that the blood of retinitis pigmentosa patients does not regularly contain a melanophore-expanding substance and that such a substance may occasionally be present in 'normal' blood.

"A further experiment is described showing that in the rabbit B-hormone injected intravenously disappears very rapidly from the circulation."

W. ZENTMAYER.

SUB-HYALOID HAEMORRHAGE FOLLOWING "T. A. B." INOCULATION. J. P. F. LLOYD, Brit. J. Ophth. **27**: 461 (Oct.) 1943.

A man aged 36, of normal physique and previous good health, received an injection of a bacterial vaccine containing 500,000,000 typhoid and paratyphoid A and B bacilli and fifteen days later a second injection containing 1,000,000,000 bacilli. Each dose produced a normal reaction. The day after the second injection he noticed that vision in the left eye was extremely poor. When he was examined two weeks later vision in this eye was limited to hand movements. An extensive subhyaloid hemorrhage lay in front of the macular region. Three months later there was considerable unabsorbed hemorrhage in the vitreous. The right eye remained normal throughout. Physical examination showed chronic bronchitis. The blood picture was normal.

W. ZENTMAYER.

DIABETIC RETINITIS. J. H. DOGGART, Brit. M. J. **2**: 212 (Aug. 14) 1943.

In a letter concerned with the diet in diabetes (*Brit. M. J.* **2**: 115 [July 24] 1943), Dr. George Graham stated: "The complication I dread in diabetes is that of retinitis and cataract. Hyperglycaemia is not the only factor in the production of these conditions, and I have seen retinitis develop in elderly diabetics although the blood sugar has been well controlled. I have much more often seen it in patients who have had an uncontrolled diabetes for some years, and I have watched the retinitis improve when the diabetic condition has been brought under control. I believe that patients who are allowed to have a blood sugar above 250 or 300 mg. throughout the day run much greater risks of this complication."

This led Doggart, in reply, to question the possibility of improvement in diabetic retinitis with treatment. In none of the cases of defective vision due to diabetic retinitis which he has seen has any appreciable restoration been shown, however soon the diabetic condition was brought under control by diet or other measures. He put the question to a number of his ophthalmologic colleagues, and none of them remembered having seen improvement in defective vision attributable to diabetic retinitis. Doggart suggests that appreciable improvement in diabetic retinitis must be extremely rare as compared with the deterioration of vision, which progresses steadily in spite of all known means of adjusting the victim's disordered metabolism.

ARNOLD KNAPP.

DIABETIC RETINITIS. R. D. LAWRENCE and WILFRID OAKLEY, Brit. M. J. 2: 312 (Sept. 4) 1943.

The authors, who are associated with the diabetes clinic, King's College Hospital, think that the difference in the experience of Mr. J. H. Doggart and Dr. George Graham (*Brit. M. J.* 2: 212 [Aug. 14] 1943) can be explained by the fact that the latter are referring to different phases of the same disease. When the usual case comes to the attention of the ophthalmologist because of defective vision, the disease is well advanced and extensive exudates are present, which can rarely be influenced by treatment. On the other hand, in the routine ophthalmic examination of diabetic patients much earlier stages of retinitis are frequently seen, with hemorrhages and small exudates, and these patients are often kept under observation for five or more years without appreciable change in vision being evident; in fact, the earliest stage, that of small hemorrhages, may completely disappear under vigorous treatment with insulin.

Of 1,500 diabetic patients with retinal lesions, 50 have lost all hemorrhages or show an occasional small one from year to year, without injury to vision. In the vast majority, many of them with large exudates, the condition of the eyes has become slowly and progressively worse, total blindness, however, being rare; in an unfortunate small minority, often among the fairly young with well controlled diabetes, retinitis proliferans has mysteriously developed, with rapid loss of vision. The rare cases of retinitis in adolescents have usually been among those whose disease was uncontrolled, the retinal lesions having developed during the worst phase, and the retinal complication was then checked by better control of the diabetes. The authors conclude that careful treatment of diabetes is most important; it may even remove the retinal condition, but more often only checks its progress.

ARNOLD KNAPP.

Tumors

EPITHELIAL TUMORS OF THE LIMBUS. J. E. ASH and H. C. WILDER, Am. J. Ophth. 25: 926 (Aug.) 1942.

From a study of 93 pure epithelial tumors arising at or near the limbus, Ash and Wilder draw the following conclusions:

"1. Epithelial 'tumors' of the limbus in adults are frequently simply leukoplakic metaplasia of conjunctival epithelium.

"2. Papilloma or squamous-cell carcinoma may develop secondarily in this altered epithelium.

"3. Basal-cell carcinoma is rare at the limbus.

"4. The tendency is to involvement of the corneal epithelium rather than to extension peripherally.

"5. Penetration of the sclera and metastasis are rare even in large carcinomas.

"6. The pathologic diagnosis of 'carcinoma' is not necessarily an indication for irradiation in connection with radical surgery. Enucleation of the eye appears

to be justified only where there is already appreciable involvement of the cornea, or after local excision has failed.

"If one must have a cancer, the limbus would seem to be as safe a place as any to have it." W. S. Reese.

Orbital Metastasis from Tumor of the Pancreas. H. R. Sniderman, Am. J. Ophth. **25:** 1215 (Oct.) 1942.

Sniderman briefly reviews the literature of carcinoma of the orbit and reports 2 cases of primary carcinoma of the pancreas with orbital metastases. In both cases the left orbit was involved and the first symptoms were diplopia. Reports of necropsy are given. W. S. Reese.

Krőnlein Operation for a Case of Cyst of the Optic Nerve. J. Hansraj, Indian J. Ophth. **4:** 6 (Jan.) 1943.

A middle-aged woman had noticed gradually increasing protrusion of the right eye, with loss of vision. There was pronounced exophthalmos, with bulging of the conjunctiva in the lower cul-de-sac and restricted movements of the globe. Vision consisted in ability to count fingers at 5 feet (152 cm.). There was papilledema. A roentgenogram showed that the right orbit was larger than the left. A Krőnlein operation was performed, and when Tenon's capsule was incised fluid escaped. Further dissection revealed a cyst the walls of which were firmly adherent behind the inner surface of Tenon's capsule. Later the exophthalmos returned. A long bent needle was passed into the retrobulbar region, and 3 cc. of fluid was withdrawn. The condition recurred and was treated in the same manner, with apparent cure. Visual acuity was 6/6. W. Zentmayer.

Vision

Visual Problems: Certain Assumptions and Data. W. T. Hunt and E. A. Betts, Am. J. Ophth. **25:** 1084 (Sept.) 1942.

After a study of 126 fifth grade pupils, Hunt and Betts summarize their results and make the following conclusions:

"The findings of this study indicate clearly the need for additional studies on the seeing problems of individuals at various age levels. These problems should be defined by means of comprehensive visual-analysis techniques. Studies reported heretofore have been cursory in nature.

"If the findings reported herein are verified by subsequent studies, then serious thought should be given to preventive measures. It may become necessary to appraise the near-point seeing tasks imposed upon elementary school children. Sustained reading activities may produce visual inefficiency, especially among school children.

"Evidences of toxic conditions uncovered in this study lead to the conclusion that the relationship between health factors and efficient seeing should be studied. In the larger sense, seeing is a psycho-physiologic process. Strictly anatomic concepts of seeing appear to circumscribe thinking and practice."

W. S. Reese.

Night Blindness, Improvement with Vitamin D: Including Experimental Production of Retinitis Pigmentosa and Its Treatment in Humans with Vitamin D. A. A. Knapp, U. S. Nav. M. Bull. **41:** 373 (March) 1943.

Knapp states that of all ocular conditions giving rise to night blindness, retinitis pigmentosa stands at the forefront. Fortunately, it is a rare disease. Night blindness may be caused by a deficiency of at least two vitamins, A and D. Another condition often complicated by night blindness is myopia. Of 93 patients with various

degrees of myopia, 64 complained of poor vision under conditions of reduced illumination. As routine treatment these 64 patients were given 60 drops (13,860 U. S. P. units of vitamin D) of synthetic oleovitamin D U. S. P. and at least 1 Gm. of available calcium. With some the dose of synthetic oleovitamin D was increased to 200 drops daily. After six to twenty-seven months of observation, during which time the patients were examined at least once a month, 20 patients showed actual reduction of the myopia. Casts of the anterior segment of many of the eyes, and in 1 instance a photograph of the fundus before and after treatment, proved beyond doubt that both the anterior and the posterior segment of the eyeball may shrink after treatment with vitamin D and calcium. Of the 64 persons suffering from poor vision at night, 48 noticed distinct improvement with respect to their nyctalopia which was in no way dependent on their myopic status. Several weeks usually elapsed before clinical improvement was definite. The majority of the patients whose myopia was reduced spoke of their greater ability to see after nightfall, and others had better vision at night when their myopia was stationary, or even in the presence of an increase in their near sightedness. The condition of 16 patients apparently remained the same. During the treatment of both the patients with retinitis pigmentosa and those with myopia toxicity was watched for. Seldom did a toxic sign develop—a mild rash, nausea, vomiting or constipation might appear—but these symptoms disappeared soon after the medication was discontinued or reduced.

J. A. M. A. (W. Zentmayer)

A Standardized Color-Vision Testing Lantern (II), Transport Type. L. C. Martin, Brit. J. Ophth. **27:** 255 (June) 1943.

A modification of the standardized color vision–testing lantern designed by Martin in 1939 has been made to render it suitable for use in transport undertakings. Experience has shown, however, that the mariner's test was a satisfactory one. The modification consists of an orange-yellow filter in addition to the original red, green and white of the first form, so that pairs of red and orange and orange and green lights can be shown. Trials with the smallest apertures and standard conditions then showed that normal persons with good color vision sometimes made mistakes—for example, a combination of green and orange might be called "green-red" or one of orange and red be called "white-red." It is necessary, therefore, when the smallest apertures (0.02 inch [0.05 cm.]) are used to restrict the lights shown to red, green and white, as in the well established mariner's test; this is even more important when the modifying glasses are used with the small apertures.

When the apertures were enlarged to a diameter of 0.05 inch (0.13 cm.), the distinctions were easy with normal vision, and this suggested the use of a diameter of 0.04 inch (0.1 cm.) as a standard for the pairs of apertures with which the supplementary part of the test are conducted.

W. Zentmayer.

Therapeutics

General and Local Administration of Penicillin. M. E. Florey and H. W. Florey, Lancet **1:** 387 (March 27) 1943.

The first part of this paper deals with various methods of administration of penicillin in cases of osteomyelitis, septicemia, empyema and subacute bacterial endocarditis. Intramuscular injection was found to be a safe, and the most practical, method of administration.

The local application of penicillin, which is discussed in the second part of the paper, is concerned chiefly with external infections of the eye. Treatment consisted of repeated application of ointments, and occasionally of aqueous solutions, containing calcium penicillin in a strength of 600 to 800 units per gram. In the 46 cases of blepharitis, chiefly infections with Staphylococcus aureus, the response

was good, but apparently no previous treatment had been attempted. In 7 cases recurrence of the infection cleared up with continued treatment. In 18 cases of acute conjunctivitis, in 6 of which the infection was complicated by corneal ulcer, Staphylococcus albus, Staph. aureus and Bacillus coli were listed as causative organisms. Of 5 cases of ophthalmia neonatorum, Staph. aureus was found in 2 and the gonococcus, B. coli and an unknown organism in 1 each of the remaining cases. The corneal ulcers healed in five to seven days except in 2 cases, in 1 of which there occurred a hypopyon of unknown origin and in the other a ring ulcer due to B. coli. The conjunctivitis disappeared in one to five weeks, and the ophthalmia, within one week.

In the 19 cases of chronic conjunctivitis the condition had not responded to previous treatment, lasting one month to several years; in all but 1 of these cases recovery was obtained with penicillin in one to nine weeks. In 6 cases of dacrocystitis a solution of penicillin was injected five times a week. Cultures taken on the eighth day were sterile, and clinical recovery occurred in 3 cases.

The authors emphasize the necessity of repeated applications of penicillin at short intervals in order to obtain a rather constant bacteriostatic concentration of the drug. It is advisable to continue the treatment for some time after an apparent clinical cure.

L. von Sallmann.

Society Transactions

Edited by Dr. W. L. Benedict

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

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Nov. 15, 1943

Spielmeyer-Vogt Disease: A Study of Its Pathology. Dr. Isadore Givner and Dr. Leon Roizin (by invitation).

Monocular Exophthalmos Due to Hyperthyroidism in a Patient with the Duane Syndrome. Dr. W. Guernsey Frey.

A white woman aged 48 presented the Duane syndrome in the left eye. There were absence of abduction, narrowing of the palpebral fissure and retraction of the globe on her looking to the right. The movements of the right eye were normal.

A toxic goiter developed three years ago, followed a year later by exophthalmos, which was more prominent in the right eye. Thyroidectomy relieved all the symptoms of hyperthyroidism except the exophthalmos, which measured 28 mm. in the right eye and 25 mm. in the left eye. The sclera was not exposed above or below the cornea in either eye. The lids were incompletely closed during sleep, but the cornea was not exposed. The lids of the left eye showed brawny edema or fatty swelling. Vision remained 20/25 in both eyes without correction.

With the development of exophthalmos, the fibrous condition of the external rectus muscle of the left eye probably interfered with the circulation of the lids, with resultant edema and swelling. It also prevented the exophthalmos from being as prominent as that of the other eye.

The case is reported as one representing a hitherto unrecorded cause of monocular exophthalmos.

Changes in the Fundus of the Eye Associated with Various Forms of Arterial Hypertension. Dr. Herman Elwyn.

This paper will be published in full, with discussion, in a later issue of the Archives.

The Ocular Fundus in Urologic Disease Associated with Systemic Hypertension. Dr. Martin Cohen.

This paper will be published in full, with discussion, in a later issue of the Archives.

Ocular Changes Associated with Experimental Renal Hypertension. Dr. Irving Graef and Dr. Robert K. Lambert.

Experimental renal hypertension was induced in 35 dogs by the application of a Goldblatt clamp to the renal arteries or by a constricting envelope of cellophane or silk about the kidneys. The dogs were prepared by Dr. Irvine Page. The ocular effects were compared with those in cases of neurogenic hypertension, bilateral nephrectomy and nephrotoxic nephritis. Normal dogs were used as controls.

Acute malignant hypertension was manifest in 23 dogs as increased blood pressure (extreme in 11 dogs and inconstant in 9 dogs), retention of urea nitrogen (20 dogs) and acute necrotizing arteriolitis in the viscera (all dogs). These animals were examined five to sixty-five days after preparation. Clinically, hemorrhage and retinal detachment were constant ocular lesions. The arterial lesions affected the uveal tract, both the anterior and the posterior portion. Edema and arteriolitis of the choroid were common, but not constant. The retinal "arterioles" were not altered to the same degree as were the choroidal vessels of similar size, although some capillary hemorrhages and disorganization of pigment were observed. The arterioles of the optic nerve were rarely affected, and arterioles external to the globe were never involved.

Eight other dogs which died of malignant hypertension from three months to one year after the onset of hypertension showed similar necrotizing lesions. The blood pressure was higher and more sustained in these animals than in the dogs with more acute malignant hypertension, and the retention of urea nitrogen was pronounced in all the animals. Arterial lesions in the viscera were again matched by those in the eyes. In addition, hypertrophy of the media of the small ocular arteries and arterioles was seen in 2 animals of this group and in other dogs examined from two to four years later.

Ocular lesions were not noted as a result of neurogenic hypertension or after bilateral nephrectomy.

On the basis of this study, significant vascular changes in the eyes accompanying experimental renal hypertension appear to be associated usually with severe impairment of renal function and mild or severe hypertension and regularly with distinctive necrotizing lesions affecting the visceral arteries and arterioles in dogs. While retention of urea is commonly associated with malignant

hypertension, it may be insignificant in some animals; hypertension, especially in cases of the rapidly fatal form, may vary from slight to severe, or the blood pressure may fall to normal before death. The lesions in the vessels appear to be of toxic origin and are coincidental as far as retention of urea or hypertension is concerned.

In animals with the benign phase of hypertension no degenerative or sclerotic vascular lesions were encountered. Hypertrophy of the media was seen on occasion in the arteries of the choroid and iris, after benign renal hypertension of one year's duration. The retinal arterioles remained unchanged in this phase. The high frequency of hemorrhagic and necrotizing lesions in the iris and the ciliary body and processes in dogs is probably due to the peculiar arterial supply of the anterior portion of the uveal tract.

CORRECTION

In the article by Dr. H. Saul Sugar entitled "Guides in the Operative (Cosmetic) Treatment of Nonaccommodative Concomitant Squint in Adults," in the November issue (Arch. Ophth. 30: 593, 1943), the following corrections should be made:

On page 599, line 4, "0.6 prism diopter" should read "8 prism diopters," and, line 5, "resection" should read "recession."

On page 601, the first sentence of the second paragraph under "Convergent Squint" should read "When the deviation for distance is greater than that for near vision, the deviation is of the divergence insufficiency type."

In the fifth line of the paragraph with the heading "Divergent Squint," "divergence insufficiency type" should read "convergence insufficiency type."

The fifth and the last paragraph on the same page, entitled "Convergence Insufficiency Type" and "Divergence Insufficiency Type," are correct as published, but the two paragraphs should be transposed.

Book Reviews

Corneal Transplantation with Fresh, Preserved and Fixed Material: Experimental and Clinical Observations. By O. I. Shershewskaya. Price, 12 rubles. Pp. 201, with 80 illustrations. Novosibirsk, U. S. S. R., Soviet Siberia Publishers, 1940.

In this monograph Shershewskaya, senior assistant at the state institute for postgraduate and clinical study in Novosibirsk, U. S. S. R., reports the results of her experimental and clinical work on the possibility of the take and retention of transparency of formaldehyde-fixed corneal disks 4 mm. in width. The book is a comprehensive and serious review of the subject and consists of eight chapters.

The first chapter gives a detailed history of keratoplasty, starting with Reisinger's first report, in 1824, von Hippel's work on total leukoma, Zirma's famous case, in 1907, and Elschnig's work in the clinic at Prague, which served as the basis of keratoplasty all over the world. Elschnig performed 203 corneal transplantations from 1908 to 1930, with resulting transparent union of the transplant in 20 per cent. Filatov and his associates performed 455 corneal transplantations from 1922 to 1938; in 264 of these operations preserved cornea from the cadaver was used, and successful results were obtained in about 67 per cent. Castroviejo, of the United States, published his results in 80 keratoplastic operations on the human eye. Such operations are performed at present in all leading ophthalmic hospitals of the Soviet Union.

In the second chapter are reviewed the present technic of keratoplasty, fixation of the transplant, complications of the operation, instruments used, partial penetration, total keratoplasty and alloplasty (with use of an artificial cornea of inorganic material). The author gives a complete description of the methods used, with drawings to illustrate the operation and the instruments used by Elschnig, Filatov, Thomas, Castroviejo, Kraupa, Löwenstein, Löhlein and others.

The material used in the operation, the indications for keratoplasty, the postoperative course and the complications are discussed in the third, fourth and fifth chapters. In the Soviet Union conditions in the donor which contraindicate the use of corneal transplants are syphilis, miliary tuberculosis, septicemia, malignant tumors and diabetes; the age, sex and blood type of the donor are not important. The most favorable results were obtained with corneas of cadavers, preserved in whole or in citrated blood at a temperature of + 3 C. The time of preservation may be as long as fifteen days, although not more than four or five days is considered the optimal period. The transplant is kept dry in a Petri dish with the epithelial surface up. Interstitial keratitis and leukoma following scrofula, i. e., nonadherent leukoma, with a deep anterior chamber, are most favorable for successful keratoplasty; normal intraocular tension, absence of inflammation of the eye and a good physical condition are essential for satisfactory results.

The most troublesome complications are the secondary opacification of the transplant, appearance of scar tissue behind the transplant and glaucoma. The various methods of combating these complications are reviewed. Filatov obtained good results in treating the opaque transplant by additional keratoplastic work about the transplant.

The sixth chapter is devoted to the histogenesis associated with keratoplasty. A review of the subject indicates that the cornea has the quality of regeneration and that it is transplantable. Histologic observations on the transplant by various authors are cited. Saltzer's brilliant experiments in transplantation of dead organic tissue, formaldehyde-fixed corneal disks, and the investigations of other authors on regeneration of the cornea indicate two directions which union of tissues may take: (1) true transplantation, with the change in the disk (Fuchs, Ascher, Elschnig,

Filatov) and (2) gradual substitution of the transplant by the regenerated tissue of the host, the transplant thus only stimulating the surrounding corneal tissue to regeneration (Saltzer, Ribbert, Thomas, Castroviejo).

Shershewskaya's own experimental results are described in chapter 7. In her study, undertaken to verify Saltzer's experiments, she used penetrating homoplastic corneas, and the size of the corneal disk was 4 mm., instead of the 2 mm. employed by Saltzer. The enucleated rabbit eye was kept for two days in a 4 per cent concentration of solution of formaldehyde U.S.P. and then for four days in isotonic solution of three chlorides U.S.P. Thirty operations were done on 37 rabbits, all with transparent corneas; in only 2 was there leukoma after a thermic burn. Union took place in 12 rabbits; of these, transplants were transparent in 3, semitransparent in 1 and opaque in 8. The time of observation was from nine to fourteen months. The low rate of "takes" was due partly to overcrowded conditions in the animal house, as the rabbits operated on were not isolated. The take of the formaldehyde-fixed transplants confirms Saltzer's observation that after a certain time the transplant is reabsorbed and replaced by the young, regenerated fibers of the host. The results of histopathologic study, records of the operation and photographs of the eyes illustrate the experiments.

The eighth, and last, chapter is devoted to clinical observations. The author performed 35 keratoplastic operations on 32 patients; in 21 of these procedures the prognosis was unfavorable (total or partial leukoma, faulty light projections or high intraocular tension), and the operation was done because of the pressing desire of the patient. Of the 11 operations with favorable prognosis, there were 6 transparent and 4 semitransparent takes and 1 opaque one. The technic of the operation, with the author's modifications, drawings, a number of tables and detailed histories are presented.

Shershewskaya performed 5 transplantations with formaldehyde-fixed corneal disks; since it was the first attempt to perform the operation on the human eye (except in Ascher's case, in which it was unsuccessful), she used 3 patients with the most hopeless outlook and 2 with fair indications for keratoplasty. She obtained 1 opaque, 2 semitransparent and 1 transparent take, and in the fifth the transplant was lost. Thus her work with formaldehyde-treated disks on animal and human eyes proved that it was possible to obtain a take. The use of formaldehyde-treated corneal disks would solve the problem of the donor. Histologic examination of the transplants in rabbits showed no definite border, as the stroma of the host blended with the fibers of the transplant. The postoperative course with the fixed disks is similar to that of unfixed transplants.

OLGA SITCHEVSKA.

Biomicroscopy of the Eye: Slit Lamp Microscopy of the Living Eye. Volume 1. By M. L. Berliner, M.D., Assistant Professor of Clinical Surgery (Ophthalmology), Cornell University Medical College; Assistant Surgeon, New York Eye and Ear Infirmary. Price, $17.50. Pp. 709, with 512 illustrations, including 40 pages of color plates. New York: Paul B. Hoeber, Inc., 1943.

"Biomicroscopy of the Eye," written to supply instruction in the technic of biomicroscopy, fills a definite need, as there is no adequate book in English on this important subject. It not only describes the required apparatus and how to use it but gives a complete and illustrated description of the findings under normal and pathologic conditions.

Volume 1 deals with the conjunctiva, eyelids, cornea and anterior chamber; volume 2, which is to follow, will discuss the iris, vitreous and lens. After a short historical sketch, the various types of biomicroscopes are described, and their manipulation is explained. The technic, according to the author, is not as difficult as it is claimed to be. The various steps are clearly stated, and the student will obtain as much information on the use of the slit lamp as can be given in a written description. Due emphasis is placed on exact localization, which Vogt particularly stressed and which formerly was only partially possible with the means

at hand. Methods of determination of the depth of the anterior chamber are given. The excellent chapter on technic concludes with a brief summary of the best order of procedure for efficient examination of the eye with the biomicroscope. The next chapters consist of a systematic survey of the conjunctiva, the margin of the eyelids and sclera, the cornea and the anterior chamber. After review of the normal histology, the normal, noninflammatory and inflammatory conditions and tumor formations are described, with valuable references to the clinical appearance and course of disease processes. The chapter on the anterior chamber deserves mention; in it are described Kronfeld's investigations, Roenne's colloidometer, thermal convection currents and changes in the aqueous. This leads naturally to the examination of the angle of the anterior chamber, "gonioscopy," which is written by Dr. H. Saul Sugar. The development of a suitable contact glass, the focal illuminating system, a suitable microscope and the technic are fully described. Presentation of this examination, which is so important, particularly in cases of glaucoma, is admirable and confirms the belief that gonioscopy should advance knowledge of the complications that follow operations for cataract and glaucoma.

Illustrations form an all-important part of a treatise of this kind. There are 512 illustrations, including 40 pages of color plates. They are excellently selected, and the beauty of the colored drawings reflects great credit on the artist, as well as on the publisher for their successful reproduction. The author has written a scientific, comprehensive and valuable book, which will be of great assistance to every student of ophthalmology, both to the beginner and to the active practitioner.

ARNOLD KNAPP.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

resident: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6^e, France.

ecretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.

.ll correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6^e, France.

International Ophthalmologic Congress

'resident: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.

ecretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

'resident: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

?resident: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.

Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.

Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.

Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chinese Ophthalmology Society

Presdient: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.

Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.

Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.

Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.

Secretary: Prof. E. Engelking, Heidelberg.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

Hungarian Ophthalmological Society

President: Prof. I. Iwre, Budapest.

Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.

All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.

Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.

Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.

Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.

Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.

Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.

Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.

All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

Ophthalmological Society of the United Kingdom

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.

Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.

Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.

Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.

Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

Place: Oxford, England. Time: July 8-9, 1943.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.

Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.

Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.

Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President: Dr. W. Belfort Mattos, Caixa Postal, 4086, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santa Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

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Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive. All correspondence should be addressed to the President.

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

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Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York City.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
Place: Chicago. Time: June 12-16, 1944.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. James A. Babbitt, 1912 Spruce St., Philadelphia.
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Executive Secretary-Treasurer: Dr. William L. Benedict, 101-1st Ave. Bldg., Rochester, Minn.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. John Green, 3720 Washington Ave., St. Louis.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.
Place: Hot Springs, Va. Time: May 29-31, 1944.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
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President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Colin A. Campbell, 170 St. George St. Toronto.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1 1509 Sherbrooke St. W., Montreal.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

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President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:4 p. m., second Monday of each month, October to May

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloi Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave Marshfield.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Paul A. Chandler, 5 Bay State Rd Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.

Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. L. L. McCoy, 1317 Marion St., Seattle, Wash.

Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle.

Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.

Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.

Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. H. Pike, Midland, Mich.

Secretary-Treasurer: Dr. R. H. Criswell, 407 Phoenix Bldg., Bay City, Mich.

Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

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Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

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Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

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President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.

Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.

Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Ray Parker, 218 Franklin St., Johnston, Pa.

Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.

Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. C. A. Ringle, 912–9th Ave., Greeley.

Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.

Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. F. L. Phillips, 405 Temple St., New Haven.

Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: Dr. E. N. Maner, 247 Bull St., Savannah.

Secretary-Treasurer:: Dr. C. K. McLaughlin, 567 Walnut St., Macon.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. F. McK. Ruby, Union City.

Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.

Place: French Lick. Time: First Wednesday in April.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.

Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Val H. Fuchs, 200 Carondelet St., New Orleans.

Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

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Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

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President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.

Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.

Time: Second Friday of each month from October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President: Dr. William Morrison, 208 N. Broadway, Billings, Mont.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St.. Lincoln.

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Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

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Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

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Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. Everett B. Muir, Boston Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Earl H. Phillips, 623 Judge Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President: Each member, in alphabetical order.
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Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. William B. Agan, 1 Nevins St., Brooklyn.
Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

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Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman: Dr. Shandor Monson, 1621 Euclid Ave., Cleveland.
Secretary: Dr. Carl Ellenberger, 14805 Detroit Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Alfred Cowan, 1930 Chestnut St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. H. D. Emswiler, 370 E. Town St., Columbus, Ohio.
Secretary-Treasurer: Dr. D. G. Sanor, 206 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Arthur Padillo, 414 Medical Professional Bldg., Corpus Christi, Texas.
Secretary: Dr. Edgar G. Mathis, 815 Medical Arts Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. S. F. Harrington, 921 Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Abell Hardin, Medical Arts Bldg., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

DETROIT OPHTHALMOLOGICAL CLUB

Chairman: Dr. Howell L. Begle, 2730 E. Jefferson Ave., Detroit.
Secretary: Dr. C. W. Lepard, 1025 David Whitney Bldg., Detroit.
Time: 6:30 p. m., first Wednesday of each month, November through April.

DETROIT OPHTHALMOLOGICAL SOCIETY

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President: Appointed at each meeting.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

EASTERN PENNSYLVANIA ASSOCIATION OF EYE, EAR, NOSE AND THROAT PHYSICIANS

President: Dr. James E. Landis, 232 N. 6th St., Reading.
Secretary-Treasurer pro tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.
Time: Last week in April each year.

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Felician J. Slataper, 1110-1111 Medical Arts Bldg., Houston, Texas.
Secretary: Dr. Theo. L. Holland, 611 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-Laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.
Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.
Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. Sylvester H. Welch, 102 N. Brand Blvd., Glendale, Calif.
Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time. 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.
Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Edwin C. Bach, 324 E. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.
Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashvile, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St. New Haven, Conn.
Secretary: Dr. Frederick A. Wiess, 255 Bradley St. New Haven, Conn.

New Orleans Ophthalmological and Oto-Laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg. New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Frank C. Keil, 660 Madison Ave., New York.
Secretary: Dr. Willis S. Knighton, 121 E. 61st St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Sigmund Agatston, 875–5th Ave., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.
Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. D. D. Stonecypher, Nebraska City, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.
Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. John B. McMurray, 6 S. Main St., Washington, Pa.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. R. M. Brickbauer, Shillington, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. C. C. Beisbarth, 3720 Washington Blvd., St. Louis.
Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.
Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. E. A. Orwig, 420 Madison Ave., Toledo, Ohio.
Secretary: Dr. E. W. Campbell, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. S. Bockoven, 1752 Massachusetts Ave., Washington, D. C.
Secretary-Treasurer: Dr. John Lloyd, 1218-16th St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg. 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.

ARCHIVES OF OPHTHALMOLOGY

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A NEW AID IN REMOVAL OF FOREIGN BODIES OF THE CORNEA

TOPICAL APPLICATION OF SILVER NITRATE

D. F. GILLETTE, M.D.

SYRACUSE, N. Y.

In this paper a new method of removal of foreign bodies from the superficial epithelium of the cornea is described. It is applicable to all foreign particles but is here chiefly concerned with the foreign bodies with an iron content encountered in industry. These quickly produce a rust stain, which becomes so firmly attached to the tissues that its removal often causes considerable damage to the corneal epithelium.

Injuries to the eye are the most disabling and costly of all nonfatal industrial accidents.[1] Most of them are caused by foreign bodies in the cornea.[2] Treatment should be prompt, efficient and economical, for infection delays healing, promotes scarring and may impair function, or even destroy the eye itself.[3]

The foreign bodies are usually hot[4] and cause a burn when they strike the cornea. The burn and the subsequent rust stain become firmly attached to the surrounding tissue.

The chemical composition of the stain has not been established. There are various theories. Leber[5] and Fuchs[6] called it hydrate of ferric oxide, while Gruber[7] described it as a hydroferric oxide. Gruber, moreover, produced similar stains by introducing sterile particles of iron into the cornea of cats and proved the presence of iron in them. He claimed that metallic iron and the ferrous oxide cause more irritation than the ferric oxide. He showed that even the chemically inert rust ring may, and usually does, slough out after inflammation of the epithelium.

Most ophthalmologists demand that the foreign body, burn and stain be carefully and completely removed as soon after the injury as possible. A minority, however, prefer to leave the stain, and at times even the foreign body and burn, to slough out rather than risk the added trauma of removal. This sloughing out requires a variable length of time and usually results in infection, with painful and disabling complications. The

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Presented as a candidate's thesis for admission to the American Ophthalmological Society in 1943.

1. McCannel, A. D.: Treatment of Common Eye Injuries, Minnesota Med. **24**:939-942 (Nov.) 1941 Rados, A.: The Eye, in Kessler, H. H.: Accidental Injuries, Philadelphia, Lea & Febiger, 1941, chap. 15.

2. Alvis, E. O.: The Eye in Industry, J. Indiana M. A. **34**:239-244 (May) 1941. Cabaniss, W. H.: The Importance of Prompt Treatment of Eye Injuries, J. M. A. Georgia **19**:513-515 (Dec.) 1930. Cridland, B.: Minor Injuries of the Eye in Industry, Brit. M. J. **2**: 615-617 (Oct. 5) 1929. Cross, G. H.: Ocular Injuries: Their Treatment, Arch. Ophth. **7**:357-360 (March) 1932. Garrow, A.: A Statistical Inquiry into One Thousand Cases of Eye Injuries, Brit. J. Ophth. **7**:65-80 (Feb.) 1923. Gulliver, F. D.: The Most Common Eye Injury: A Practical Consideration, read at the Fifty-First Annual Session of the New York and New England Association of Railway Surgeons, Dec. 5, 1941. Jones, C. D.: First Aid to the Injured Eye, Virginia M. Monthly **56**:96-98 (May) 1929. Miller, J. S., Jr.: Industrial Ophthalmology, Hahneman. Monthly **74**:97-107 (Feb.) 1939. Minton, J.: Industrial Eye Injuries, Indust. Welfare **20**:265-271 (July) 1938. Nutting, R. J.: Industrial Corneal Injuries, California & West. Med. **30**:344-345 (May) 1929. Vidal, J.: Infortunistica ocular, Hospital, Rio de Janeiro **20**:379-404 (Sept.) 1941. Wernner, W. T.: Foreign Bodies in Cornea: Care and Complications, Minnesota Med. **22**:28-31 (Jan.) 1939.

3. Begle, H. L.: Problems in the Care of Industrial Injuries of the Eye, J. Michigan M. Soc. **20**:443-446 (Nov.) 1921. Benedict, W. L.: Office Treatment of Eye Injuries, Wisconsin M. J. **38**:187-190 (March) 1939. Black, G. W.: Ophthalmic Emergencies, Practitioner **140**:478-488 (April) 1938. Brown, J. E.: Eye Injuries and the Workmen's Compensation Law, Ohio State M. J. **16**:909-914 (Dec.) 1920. Caldwell, R.: Industrial Eye Injuries, South. M. J. **18**:619-621 (Aug.) 1925. Campbell, D. M.: Some Phases of Industrial (Factory) Eye Surgery, J. Michigan M. Soc. **27**:666-667 (Oct.) 1928. Gifford, S. R.: Ocular Foreign Bodies: Importance of Immediate and Proper Care, Indust. Med. **6**:129-132 (March) 1937. Parsons, J. H.: Treatment of Minor Injuries to the Eye, Lancet **1**:451-452 (March 3) 1923. Patton, J. M.: The Management of Ocular Injuries, Nebraska M. J. **15**:429-432 (Nov.) 1930.

4. Walker, S., Jr., and Auten, H. L.: Industrial Injuries to the Eye: Essentials of First Aid and Late Management, J. A. M. A. **116**:1356-1357 (March 29) 1941.

5. Leber, T.: Die Entstehung der Entzündung und die Wirkung der entzündungerregenden Schädlichkeit. Nach vorzugsweise am Auge angestellten Untersuchungen, Leipzig, W. Engelmann, 1891, pp. 220-225.

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method described in this paper anticipates the localized softening of the epithelium and aids in the immediate, safe and complete removal of the foreign body, burn and stain.

METHOD

Silver nitrate has long been used in ocular therapeutics as a prophylactic, antiseptic and caustic agent. The method I describe here utilizes the chemicophysical reaction produced by the topical application of a 1 to

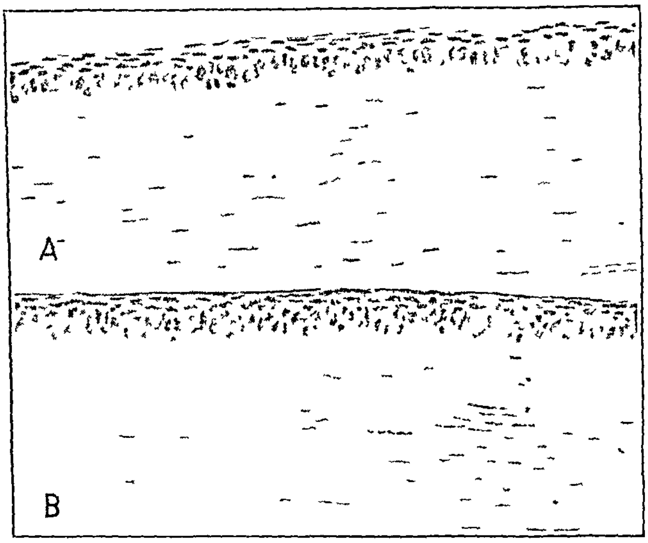

Fig. 1.—*A*, section of uninjured cornea of the rabbit eye treated with a 1 per cent solution of silver nitrate; *B*, section of the uninjured cornea of the rabbit eye treated with a 3 per cent solution of silver nitrate.

3 per cent solution of silver nitrate to the foreign body and the surrounding epithelium. The solution is applied by a small thread of cotton spun on the sharpened end of a round wooden toothpick. The cotton is cut off clean with sterile scissors so as to remove any stray fibers that might spread the solution over too large an area of the cornea.

The reaction is a faint, gray swelling of the superficial epithelium, which elevates the foreign body slightly above the level of the surrounding epithelium. This swelling appears to be caused by local softening and edema of the tissue. It has been observed that a 1 per cent solution of silver nitrate usually produces a sufficient reaction. The 3 per cent solution, which acts faster and produces a greater reaction, was used in several cases in early experiments. The reaction produced by the silver nitrate was inspected with the slit lamp and tested by experiments on animals.[8]

ANIMAL EXPERIMENTS

Normal and abraded corneas of rabbit eyes were treated topically with 1 and 3 per cent solutions of silver nitrate. The animals were killed and the corneas removed fifteen minutes after topical application of the solution. The corneas were then fixed, sectioned and stained.

8. Ferguson, J. H., in Reports from the Department of Pathology, Syracuse University College of Medicine, February, March and April 1943. Von Sallmann, L., in Report from Columbia University College of Physicians and Surgeons, Department of Ophthalmology, May 1943.

Photomicrographs of these sections of the cornea of the rabbit eye show the effect of the solutions of silver nitrate on the superficial epithelium. *A* of figure 1, a section of an uninjured cornea which was treated with a 1 per cent solution of silver nitrate, shows no definite change. In *B* of the same figure, a section of an uninjured cornea treated with a 3 per cent solution of silver nitrate, a slight amount of pigmentation is apparent in the outer layers of the epithelium.

In *A* of figure 2, a section of the abraded cornea treated with a 1 per cent solution of silver nitrate, the epithelium is pyknotic and stained with silver nitrate. In *B*, a section of the abraded cornea treated with a 3 per cent solution of silver nitrate pronounced pyknos[is] and deeper staining of the epithelium are ap[parent]. Unfortunately, the injury of the ep[i]thelium in this eye was more severe than that in the eye shown in *A*.

Figure 3 *A* shows a section of an abraded cornea of the rabbit eye which was removed and fixed fifteen minutes after the topical application of a 1 per cent solution of silver nitrate. A fine cotton applicator saturated with the solution had been kept in contact with the epithelium for one minute. The superficial layers of epithelium are necrotic and have sloughed off. Impregnation with the silver salt is seen. The basal cells which appear in place, are partly swollen and

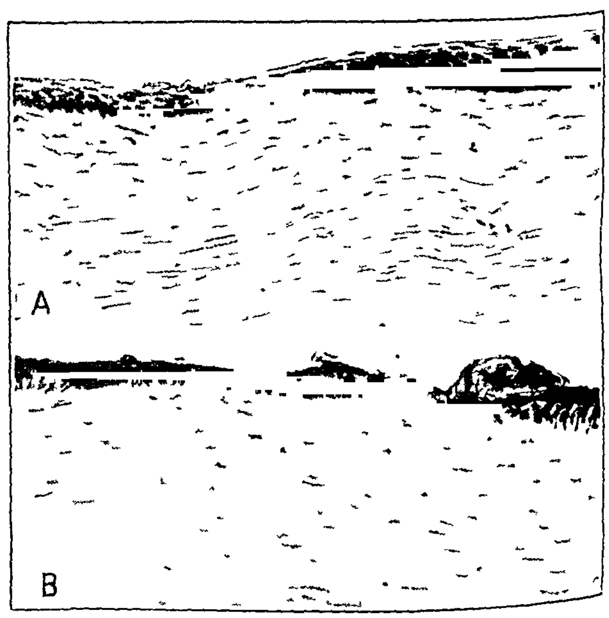

Fig. 2.—*A*, section of the abraded cornea of the rabb[it] eye treated with a 1 per cent solution of silver nitrate[;] *B*, abraded cornea of the rabbit eye treated with a 3 p[er] cent solution of silver nitrate.

partly shrunken. They are separated by inter[]stices, which are interpreted as due to edema. A few nuclei are pyknotic, and the cytoplasm has taken a darker stain. In *B* of figure 3, a section

of an abraded cornea which was removed and fixed one hour after similar treatment with a 3 per cent solution of silver nitrate, the cornea is almost denuded of epithelium, and a few shrunken cell bodies with pyknotic nuclei constitute the remnants of the basal layer. The section shows no definite changes in the stroma, and the endothelium is normal.

These observations indicate that the solution of silver nitrate had not penetrated through the cornea and substantiate reports on the pharmacologic effect of silver nitrate in burns due to the drug (such as those of the conjunctiva) in which the coagulation necrosis affects only the more superficial layers of the epithelium. Regeneration takes place in a short time. The experiments support my belief that it is best to apply the 1 per cent solution of silver nitrate for only two or three seconds.

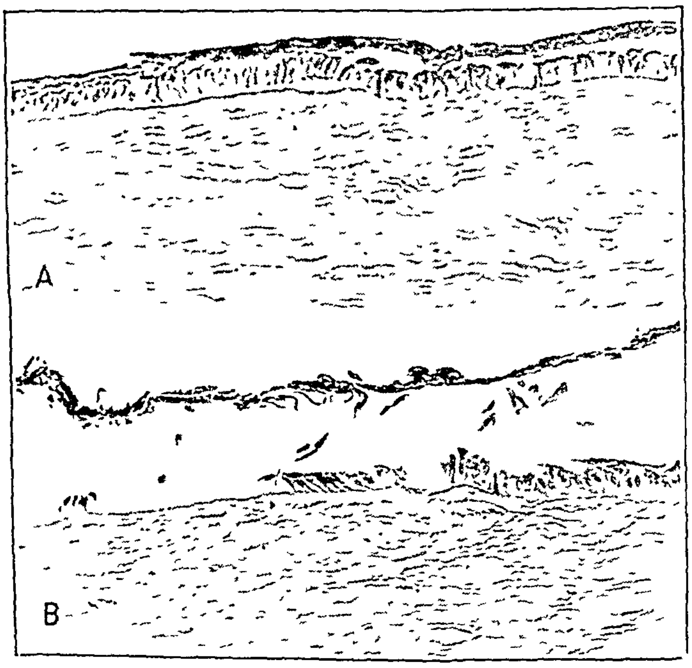

Fig. 3.—*A*, section of abraded cornea of the rabbit eye which was removed and fixed fifteen minutes after topical application for one minute of a 1 per cent solution of silver nitrate; *B*, section of the abraded cornea of the rabbit eye which was removed and fixed one hour after topical application of a 3 per cent solution of silver nitrate.

The literature on removal of foreign bodies from the cornea reveals two chemical approaches to the problem. Páez Allende[9] used a 5 per cent solution of a cocaine salt to "destroy the epithelial cells that held the foreign body." Rycroft,[10] in a case of multiple foreign bodies, instilled a 4 per cent solution of a cocaine salt into the eye until he was able to peel off the softened superficial epithelium.

9. Páez Allende, F.: Cuerpo extraño de la córnea, Día méd. **11**:626 (July 17) 1939.

10. Rycroft, B. W.: The Non-Magnetisable Metallic Foreign Bodies of the Cornea, with the Report of a Case, Brit. J. Ophth. **14**:501-505 (Oct.) 1930.

In my experimental investigation of the method I describe I placed several particles of iron in the superficial epithelium of the cornea of rabbits. The stains formed within an hour. The foreign bodies and their immediate borders were treated with a 3 per cent solution of silver nitrate. The epithelium so treated became faintly gray and edematous. The reaction elevated the foreign body on a shallow dome of swollen tissue. The foreign body and the stain were then removed with little additional trauma to the epithelium. This topical use of the silver solution did not permanently damage the epithelium, did not delay healing and did not produce a silver oxide stain that remained visible with the slit lamp.

This method, with the employment of 1 per cent solution of silver nitrate, was then tried with 3 patients with foreign bodies of the cornea. The results were so good that use of the method was continued.

CLINICAL APPLICATION

The patient was tilted back in a dressing chair, which supported his head in a firm position, and one which was comfortable for both him and the operator. The injured eye was carefully anesthetized by instillation of 1 drop of a 0.5 per cent solution of tetracaine hydrochloride at one minute intervals. Two or three instillations were usually enough to produce complete surface anesthesia. The eye was then carefully inspected with a self-illuminated binocular loupe. The use of this instrument left both the operator's hands free so that he was able to control the head and lids with one hand and use the other for the operation. The patient was instructed to keep both eyes open and fixed on a point to facilitate the inspection and operation.

The slit lamp was used to locate the minute foreign particles that could not be satisfactorily seen with the loupe. The very small dark particle located in the pupillary area of the cornea in 1 case was easily delineated by retroillumination. The conjunctival sac was irrigated with 5 or 6 drops of a mild solution of mercury oxycyanide.[11] When necessary, a drop of a sterile 2 per cent solution of fluorescein sodium was used to map an abrasion of the cornea or to outline the foreign body. The nature, size and depth of the foreign body, as well as any stain or sign of infection, were carefully noted.

The 1 per cent solution of silver nitrate was then applied to the foreign body. The reaction which developed in one minute was sufficient.

11. The solution had the following composition: mercury oxycyanide, 1.25 mg.; mercury cyanide, 2.50 mg.; boric acid, 1 per cent, 30 cc.

Removal of the foreign body was then attempted with a sterile, pointed wooden applicator, tightly wound with cotton. For the past three months I have used the sharpened end of a round toothpick. These toothpicks are kept in the steam sterilizer, so that the point is as soft as, and finer than, that of the cotton-wound applicator.

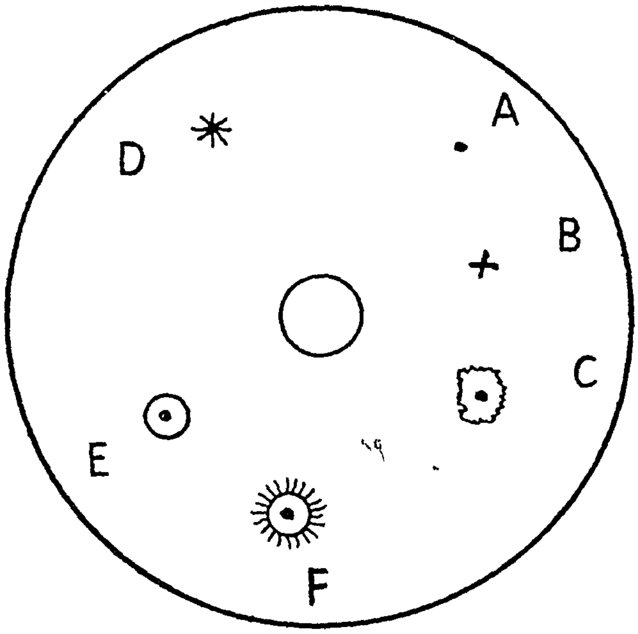

Fig. 4.—Graphic representation of the site and nature of the foreign body and local complications.

A indicates foreign body; *B*, foreign body with stain; *C*, foreign body with abrasion; *D*, foreign body with infiltration; *E*, foreign body with ulcer, and *F*, foreign body with ulcer and zone of infiltration.

This method aided the complete removal of the foreign body, burn and stain when the patient was treated soon after injury. When, however, the stain did not readily come away, the point of a cystotome was used gently to lift it out. When the patient was seen late, the foreign body and burn were easily removed, but the stain, having further penetrated the tissues, was not always dislodged with the applicator.

In the patients who were treated late the point of the cystotome was used carefully to free and lift out the stain. A cystotome, with the cutting edge removed, is an ideal instrument, for it has a fine point and requires but a slight roll of the handle to give the necessary lift to the point. It also allows a smoothness of movement not possible with the foreign body spuds or the knife needle. The cystotome produced little trauma as compared with that caused by the foreign body spud, the curet or the dental burr, each of which produces unnecessary destruction of tissue. This fact is readily demonstrated with the slit lamp. In 2 cases the stained disk was observed to be attached to the cornea by a tough pedicle. A fine, smooth forceps was used to tear these attachments away from the cornea.

Injury to Bowman's membrane was avoided for such a lesion exposes the less resistant stroma of the cornea to possible infection and always heals with scar formation. The silver nitrate procedure was not used when Bowman's membrane had been injured, for it allowed the solution to spread into the deep interspaces and produce unwanted stain.

White's ointment (crude coal tar, zinc oxide and petrolatum), or sulfathiazole ointment, 5 per cent, was instilled immediately after the removal of the foreign body and stain. When possible the eye was protected with a sterile eye patch held snugly in place with Scotch tape. In 2 cases contact dermatitis developed from the use of this adhesive.

The patient was instructed to instil some of the ointment if the eye became uncomfortable. He was asked to return on the following day with the pad in place. When iritis was present the pupil was dilated, the mydriatic used depending on the degree of the iritis, the probable length of disability and the possibility of glaucoma.

In the early part of this investigation an ulcer was cauterized with tincture of iodine. This treatment always caused such discomfort that the patient was incapacitated for work for the next six to twelve hours. During the six months, prior to the time of writing an ulcer has been cleansed of its exudate with a small cotton-wound applicator saturated with tincture of metaphen (1:200). The area was then filled with sulfathiazole powder, which was left in place one minute. The undissolved portion was washed away with the tears. This was accomplished by having the patient wink several times. Sulfathiazole ointment, 5 per cent, was prescribed for use after the powder. The patient was instructed to use the ointment and hot

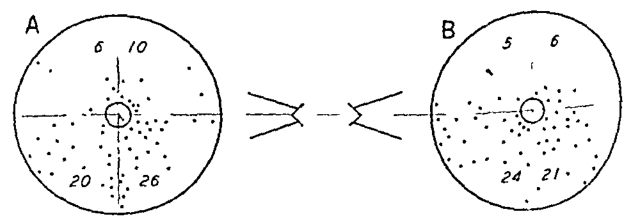

Fig. 5.—Graphic representation of the location of 118 foreign bodies occurring in 100 unselected cases of injury to the eye treated by the method described.

A shows 62 foreign bodies in the right eye (55 cases), and *B*, 56 foreign bodies in the left eye (45 cases).

compresses to relieve any discomfort. Several drops of the weak solution of mercury oxycyanide were instilled to flush the conjunctival sac

when the eye showed any evidence of secretion. Such a potentially infected eye was also treated with a topical application of the sulfathiazole powder. This powder gave good results and was much less irritating than the tincture of iodine. The eyes treated by the silver nitrate method soon after injury healed quickly and without formation of scar. This was so evident that intelligent patients were allowed to remove the dressing if the eye had been comfortable for two hours after treatment by this method.

The patient with signs of infection was ordered to go home and was instructed to apply hot compresses and to instil drops of the weak solution of mercury oxycyanide at regular intervals. The frequency of treatment depended on the pain and the degree of infection. The patient was also instructed to instil White's or the sulfathiazole ointment into the eye after each treatment with the solution and to replace the patch unless, as sometimes happens, it increased the pain. In this event he was told to wear the black glasses which were furnished him.

The ophthalmic examination and record were made as complete as possible at the patient's first visit and were finished as soon as the condition of the eye permitted. The site and nature of the injury were graphically recorded, as indicated in figure 4. In figure 5 are represented the sites of the 118 foreign bodies occurring in 100 unselected cases in which this method of treatment was used. The diagram shows that the great majority of the foreign bodies were located in the middle portion of the lower half of the cornea. This area represents the interpalpebral space when the patient is looking slightly down, as at his work.

COMMENT

Table 1 shows that by far the greatest number of injuries from foreign bodies in the cornea are incurred before the abrasive wheel, but many are obtained at machining tools, such as the lathe and shaper. In table 2 is recorded the time which elapsed between the injury and the treatment. The cases are divided into convenient groups on this basis. In table 3 are shown the number of cases in each time group in which the cotton-wound or soft-pointed applicator was successfully used and the number in which employment of the cystotome was required. Table 4 shows the average period of disability for each time group and demonstrates the economy of early, careful treatment. The values were determined on the basis of a twenty-four hour day because number of work hours was variable as a result of necessary periods of overtime work.

Table 1.—*Occupation at Time of Injury*

	No. of Cases
Operation of abrasive wheel	44
Machining of tools, such as lathe and shaper	19
Hammering, chipping, etc.	8
Cleaning casting with wire brush	8
Cleaning up with air hose	9
Welding	1
Miscellaneous work	11

Table 2.—*Interval Between Injury and Treatment*

Time Group, Hours	No. of Cases
0- 6	36
6-12	19
12-24	26
24-48	8
48-72	8
72 plus	3

Table 3.—*Analysis of Methods of Treatment Required on Basis of Time After Injury*

Time Group (Hours After Injury)	Cotton Applicator		Cystotome	
	Number	Percentage	Number	Percentage
0- 6	34	94.4	2	5.6
6-12	8	42.0	11	58.0
12-24	7	27.0	19	73.0
24-48	0	0.0	8	100.0
48-72	1	12.0	7	88.0
72 plus	0	0.0	3	100.0

Table 4.—*Average Number of Days of Disability per Group*

Hour Groups	Days of Disability
0- 6	0.027
6-12	0.421
12-24	0.73
24-48	0.80
48-72	1.62
72 plus	4.00

CONCLUSIONS

The topical application of silver nitrate before removal of foreign bodies from the cornea is of value for these reasons: (*a*) It facilitates removal of the foreign body, burn and stain from the corneal epithelium; (*b*) it causes a minimum amount of trauma, and (*c*) it is economical, for it conserves time and function. The results indicate that the earlier the patient is treated the more successful is the method.

Dr. Arnold Knapp and Dr. Ludwig von Sallmann, of the Institute of Ophthalmology, New York, and Dr. J. H. Ferguson and Dr. M. S. Dooley, of the faculty of Syracuse University College of Medicine, gave advice in this investigation.

109 South Warren Street.

A WORD OF CAUTION IN USE OF PENTOTHAL SODIUM IN OPHTHALMIC SURGERY

HAROLD F. FALLS, M.D.*

ANN ARBOR, MICH.

Pentothal sodium, a short-acting barbiturate, has been widely employed as an anesthetic for intravenous administration during the past few years. The large number of articles currently appearing in scientific journals concerning its use indicates that the drug is now occupying the crest of its wave of popularity. Pentothal sodium is a powerful and rapidly acting drug, which may be employed for operations requiring only analgesia or procedures of short duration. It should be administered only by persons trained and experienced in its pharmacologic action and in specific resuscitative procedures. The drug is potentially dangerous, since it is a depressant of the respiratory center in the medulla. Recent experimental work [1] indicates that pentothal sodium effects an early loss of precise control of breathing and of the acid-base equilibrium. This depressant action of pentothal sodium on respiration should restrict its use to short, relatively atraumatic operative procedures.

Many ophthalmologists have been prone to accept pentothal sodium without reservation. Its use in ophthalmic operations is rapidly becoming general. The freedom of the ophthalmic operative field granted by use of the drug is to be commended as well as the ease and rapidity of induction. Without a complete analysis of the results of its use, pentothal sodium would seem to be an ideal anesthetic for ophthalmic surgical procedures, and in the great majority of cases this may be true. It is the purpose of this paper, however, to report untoward reactions and complications encountered during and after the administration of pentothal sodium in 147 cases in which ophthalmic operations were carried out at the ophthalmic clinic from July 1940 to March 1943. A short discussion of 1 case of death and of several cases of apnea encountered during and after operation, as well as of procedures employed to combat this complication, is included.

METHOD OF ADMINISTRATION

The slow, intermittent method of induction and the intermittent administration of supplemental doses as required constitute the accepted method.[2] The drug must not be given too rapidly. A 2.5 per cent solution of pentothal sodium in water has been found to be the most satisfactory concentration. The continuous administration of oxygen, with or without supplemental nitrous oxide, is now recommended by nearly all anesthetists and surgeons. Premedication is the practice of the great majority of anesthetists. The most satisfactory premedicaments are morphine sulfate and atropine sulfate, given hypodermically. The dose must be individualized according to such factors as weight, constitutional status and basal metabolic rate. It is thought best to give atropine sulfate fifteen to thirty minutes before induction of anesthesia is initiated. Morphine sulfate may be given one to one and one-half hours before operation. The latter drug is thought to increase the analgesia and reduce the amount of pentothal sodium required, as well as to prevent excitement and muscular activity during and after induction. Atropine or scopolamine effects paralysis of the parasympatheticomimetic action of intravenously administered barbiturates, so that excess mucus and pharyngeal and laryngeal spasm are reduced. The ophthalmologist will find it necessary to instil 1 drop of a 4 per cent solution of cocaine hydrochloride into each eye at five minute intervals before beginning the administration of pentothal sodium to avoid reflex vagal sneezing and coughing on stimulation of the fifth nerve.

CONTRAINDICATIONS

Intravenous anesthesia is not practical or safe for children, since the margin of safety is small and large amounts are necessary to effect analgesia. Obese subjects are difficult to anesthetize because of the small, deep, hidden veins. The site and method of destruction of the drug are not known, and until investigation clarifies this process it is felt that nephritic and hepatic disease are contraindications to the use of the drug. Increased intracranial pressure, because of the associated depression of respiration, prohibits the use of a respiratory depressant. Pentothal sodium is not suitable for long surgical procedures which require adequate muscular relaxation.

REVIEW OF CASES OF OPHTHALMIC SURGICAL PROCEDURES

A total of 147 consecutive and unselected cases in which ophthalmic operations were carried out provided the material for this review. Division of this number on the basis of sex revealed that in 80, or 54.41 per cent, the patients

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* Walter R. Parker Scholar, University of Michigan Medical School.

1. Beecher, H. K., and Moyer, C. A.: J. Clin. Investigation **20**:549-566 (Sept.) 1941.

2. Lundy, J. S.: Clinical Anesthesia, Philadelphia, W. B. Saunders Company, 1942.

were males and in 67, or 45.59 per cent, they were females. The average age was 35.52 years. The youngest patient was 7 years and the oldest 83 years of age.

TABLE 1.—*Various Procedures Employed in One Hundred and Forty-Seven Ophthalmic Operations*

Surgical Procedure	No. of Cases	Percentage
Operations on extraocular muscles	52	35.36
Iridectomy	9	6.12
Enucleation	24	16.32
Cataract extraction	7	4.76
Linear cataract extraction	1	0.68
Conjunctivoplasty	7	4.76
Removal of biopsy specimen of orbital tumor	3	2.04
Evisceration	15	10.20
Frost suture	1	0.68
Dacryoconjunctivorhinostomy	1	0.68
Paracentesis	2	1.36
Implantation of vitallium ball	1	0.68
Dacryocystorhinostomy	2	1.36
Plastic repair	2	1.36
Extirpation of lacrimal sac	5	3.40
Exenteration	5	3.40
Trephination	4	2.72
Cyclodiathermy	1	0.68
O'Connor transplantation	1	0.68
Needling	1	0.68
Dilatation of lacrimal sac	1	0.68
Dressing of orbit	1	0.68
Incision and drainage of lacrimal sac	1	0.68

The average amount of pentothal sodium administered in each case was 37.48 cc. of the 2.5 per cent solution. The greatest single amount administered was 118 cc. The average duration of anesthesia was thirty-four and twenty-one-hundredths minutes. Thus, approximately 1.09 cc. of a 2.5 per cent solution of pentothal sodium was administered per minute per case.

TABLE 2.—*Operative Course in One Hundred and Forty-Seven Ophthalmic Operations in Which Anesthesia Was Induced with Pentothal Sodium*

Operative Course	No. of Cases	Percentage
Satisfactory	97	65.96
Formation of airway necessitated	8	5.44
Coughing	8	5.44
Laryngeal spasm	1	0.68
Cyanosis	5	3.40
Light anesthesia used	5	3.40
Sneezing	6	4.08
Large amount of pentothal sodium required for induction	15	10.20
Apnea	8	5.44
Artificial respiration required	6	4.08
Straining	6	4.08
Shallow and poor respiration	5	3.40
Extrasystoles	3	2.04
Death	1	0.68
Very moist rales	3	2.04

The ophthalmic operations included twenty-three procedures, of which operations on ocular muscles, enucleations, eviscerations, conjunctivoplastic procedures and extractions of cataracts constituted the greater percentage (table 1).

In 97, or 65.96 per cent, of the cases there was no complicating incident during induction of anesthesia or operation. In 15, or 10.21 per cent, of the cases large amounts of pentothal sodium were required for induction of anesthesia. It is suggested that other anesthetic agents should be employed when induction is difficult and large quantities are required. Coughing or sneezing was present in 9.52 per cent of cases. Adequate cocainization of the cul-de-sac has greatly reduced this complication during the past two years (table 2).

Apnea occurred in 8 cases, in 1 of which it terminated in death.

REPORT OF EIGHT CASES IN WHICH APNEA OCCURRED

CASE 1.—A Negro aged 76 was subjected to enucleation for a painful secondary glaucoma. Apnea immediately followed removal of the eye or appeared on cessation of the painful stimulation of respiration incident to operation. The heart continued to beat for a short period after respiration ceased. Artificial respiration, administration of oxygen under pressure, intracardiac injection of epinephrine, injection of nikethamide and painful peripheral stimulation failed to restore respiration, and death occurred in four minutes. A limited postmortem examination failed to show any damage that might have been produced by the pentothal sodium itself. Severe, generalized arteriosclerosis and arteriosclerotic heart disease were present. It is believed that the painful stimuli from the eye were sufficient to keep the respiratory rate at a level which did not awaken suspicion during the operation even though an overdose of pentothal sodium had been given. The true situation became evident only when the abnormal respiratory drive provided by the "painful" stimuli stopped. The administration of 100 per cent oxygen under pressure after the apnea became apparent may have further depressed respiration as a result of the anoxia-allaying action of a relatively high arterial oxygen tension on the carotid body.

CASE 2.—A white man aged 64 was subjected to evisceration of the eye for chronic iridocyclitis. Momentary apnea was displayed during the early stage of induction of anesthesia, after 12 cc. of a 2.5 per cent solution of pentothal sodium had been injected. Spontaneous respirations were resumed when further injection was withheld. Too rapid induction of anesthesia was probably responsible for the apnea.

CASE 3.—A well developed, muscular youth aged 18 was subjected to surgical correction of strabismus. Apnea of short duration was manifested on injection of 9 cc. of a 2.5 per cent solution of pentothal sodium. Respiration was resumed spontaneously, and the operative course was otherwise uneventful. It was believed that in this case, too, induction of anesthesia was too rapid.

CASE 4.—A white woman aged 52 was subjected to evisceration of the right eye for panophthalmitis. No premedication had been given this patient, who was extremely apprehensive. Severe apnea immediately followed evisceration of the ocular contents. Artificial respiration, administration of 100 per cent oxygen and intravenous injection of nikethamide were employed to restore spontaneous respiration. It is now recognized that administration of 100 per cent oxygen was dangerous in this case because of its effect on the control of breathing by the carotid sinus reflex.

Case 5.—A man aged 62 was subjected to enucleation for *endophthalmitis.* The procedure lasted thirty-five minutes, and a total of 45 cc. of a 2.5 per cent solution of pentothal sodium was administered. The operative course was uneventful, but shortly after he returned to the ward respiration ceased. Artificial respiration and intravenous injections of nikethamide and picrotoxin were employed to restore spontaneous respiration. The patient did not react for two and one-half hours and was very drowsy for at least sixteen hours longer. This case emphasizes the point that careful postoperative observation of the patient is a necessary part of pentothal sodium anesthesia.

Case 6.—A white man aged 52 with arteriosclerotic heart disease was subjected to exploration of the right orbit in order to obtain a specimen of an orbital tumor for biopsy. Respirations became shallow soon after initiation of the operation, and two momentary periods of apnea were encountered. The operation lasted one hundred minutes, 80 cc. of a 2.5 per cent solution of pentothal sodium being injected during that period. It is believed that the depression of respiration in this case resulted from the large amount of the drug employed during the long surgical procedure. The patient did not react for four hours after operation.

Case 7.—A white woman aged 35 was subjected to enucleation of the left eye for secondary glaucoma following intraocular hemorrhage. The patient had severe essential hypertension, the blood pressure being 240 systolic and 150 diastolic. Intravenous administration of pentothal sodium was chosen because of the fall in blood pressure reported in cases of essential hypertension; it was believed, therefore, that the patient would do best with this anesthetic. A minor degree of apnea was experienced after 10 cc. was injected. This was quickly overcome by administration of a combination of nitrous oxide and oxygen. A second, more serious, period of apnea followed removal of the eye. Spontaneous respiration was restored by the use of artificial respiration, nikethamide and a mixture of nitrous oxide and oxygen. The patient did not respond for two and one-half hours. Severe nausea and vomiting persisted for several hours after response was obtained. The patient died sixteen days after operation. The postmortem examination revealed severe hypertensive heart disease and pyelonephritis. No connection between the previous administration of pentothal sodium and the cause of death was determined.

Case 8.—A white boy aged 7 years was subjected to exenteration of a large spindle cell sarcoma of the left orbit. The patient had had no premedication. A brief induction of anesthesia was followed by a satisfactory course until the operation was nearly completed. Momentary apnea appeared, which was relieved by artificial respiration. The patient did not fully respond until the next day and showed evidences of shock. The pulse was rapid; the respirations were shallow, and the color was poor. A blood transfusion, together with other supportive treatment, was administered. The operation lasted for ninety minutes, during which 50 cc. of the 2.5 per cent solution of pentothal sodium was injected.

It must be admitted that in the majority of these cases apnea was the sequela of errors in the technic of administration, and perhaps in the choice, of the anesthetic. It is desired that these cases shall serve as examples of such error and that similar mistakes will be avoided in the future.

In a rather high proportion, 10.21 per cent of the cases a large amount of pentothal sodium was required for induction of anesthesia. It is urged that the anesthetist change to inhalation anesthesia when it is apparent that the patient is resistant to the effects of the drug.

EFFECTS OF PENTOTHAL SODIUM ANESTHESIA

Postoperative Complications (table 3).—The relative freedom from postanesthetic complications after employment of pentothal sodium has

Table 3.—*Incidence of Postoperative Complications After Use of Pentothal Sodium Anesthesia in One Hundred and Forty-Seven Ophthalmic Operations*

Postoperative Course	No. of Cases	Percentage
Satisfactory	54	36.72
Restlessness	23	15.64
Emesis	26	17.68
Period before response was obtained		
1 hour	8	5.44
2 hours	6	4.08
3 to 5 hours	8	5.44
Coughing	5	3.40
Nausea	36	24.48
Severe headache	2	1.36
Apnea	2	1.36
Artificial respiration required	3	2.04
Respiration shallow	4	2.72
Patient irrational and difficult to handle	2	2.04
Profuse sweating	1	0.68

been stressed by many authors,[3] but, as an ophthalmologist, I view with alarm the high percentage of cases of nausea (24.48) and emesis (17.68) in this series. Postoperative nausea and emesis are difficult to evaluate when one is analyzing the effects of pentothal sodium, since psychic influences, nervous tension and sensitization to drugs used in premedication must be considered. Even granted the necessity of occurrence of the aforementioned complications, it is felt that the percentages are higher than those observed after similar procedures performed with local anesthesia. Nausea and emesis are serious postoperative complications of ophthalmic operations, particularly intraocular

Table 4.—*Effect on Respiration of Pentothal Sodium Anesthesia in One Hundred and Forty-Seven Ophthalmic Operations.*

Respiratory Rate	No. of Cases	Percentage
Rise: 3-6 (moderate)	23	15.64
Over 6 (pronounced)	23	15.64
Fall: 3-6 (moderate)	10	6.80
Over 6 (pronounced)	6	4.08
No essential change	85	57.80

3. Long, C. H., and Ochsner, A.: Surgery 11:474 (March) 1942.

procedures, because of the damaging sequelae of the resultant suddenly increased intraocular pressure.

The prolonged postoperative period of reaction, present in nearly 14.96 per cent of cases, is the result of the rather large doses of pentothal sodium employed. Careful nursing care is required during this state of unconsciousness. Passage of air must be maintained, and frequently the chin must be supported to avoid respiratory embarrassment. Prompt relief of apnea by appropriate resuscitative measures is necessary to avoid death.

Pulse Rate (table 5).—In general, the pulse rate increased slightly during the administration of pentothal sodium. However, individual variations in this respect were encountered.

Blood Pressure.—The blood pressure increased to a minimal degree early in the course of the anesthesia but later tended to fall slightly below the original level.

Table 5.—*Effect on Pulse Rate of Pentothal Sodium Anesthesia in One Hundred and Forty-Seven Ophthalmic Operations.*

Pulse Rate	No. of Cases	Percentage
Rise: 5-19 (moderate)	45	30.60
Over 20 (severe)	20	13.60
Fall: 5-19 (moderate)	26	17.68
Over 20 (severe)	11	7.48
No essential change	45	30.60

SUGGESTED REGIMEN FOR RESUSCITATION OF PATIENTS IN APNEA

When respiratory failure occurs during pentothal sodium anesthesia, artificial respiration by thoracic pressure is indicated.[4] A gas mixture containing not more than 40 per cent oxygen and not more than 4 to 5 per cent carbon dioxide should be administered, but positive intratracheal (intrapulmonary) pressures are not to be employed. When cardiac failure appears imminent or the blood pressure is low, 2 to 4 minims (0.13 to 0.26 cc.) of epinephrine hydrochloride (1:1,000) should be given intravenously.

These principles were evolved after careful animal experimentation had revealed much that could be applied to human anesthetization. It was found that pentothal sodium effects a profound depression of the stimulating action of carbon dioxide on the respiratory center. This effect has been observed either with or without the use of morphine as a premedicament. Henderson evolved the term anarchapnea for the level of pentothal sodium anesthesia in which the corneal and sciatic reflexes are active and respiration can be driven effectively by reflex stimulation (proprioceptive and chemosensitive). Obviously, the intermittent administration of high oxygen concentrations will reduce the effectiveness of the latter reflex control. In fact, breathing may fail if the administration of a high concentration of oxygen should suddenly be initiated during the time that respiration is under the control of the chemosensitive (carotid sinus) or proprioceptive (vagal) reflexes. Administration of oxygen must be continuous to be safe and of value and must be started before the induction of pentothal sodium anesthesia is initiated.

Pressure on the thoracic wall expels gas from the lungs and provokes proprioceptive impulses and, if strong enough, will stimulate the respiratory center to effect return of spontaneous respiration.

Epinephrine may be necessary to provide an adequate volume flow of blood, the purpose being to provide the brain with oxygen and to remove carbon dioxide.

4. Moyer, C. A.: J. Thoracic Surg. 2:131-150 (Dec.) 1941.

SUMMARY

Pentothal sodium is a barbiturate and, as such, is endowed with considerable variability of action. Among the chief effects of intravenous administration of the drug is depression of the respiratory center in the medulla.

The lack of adequate signs of impending respiratory failure makes the margin of safety too narrow to permit unqualified use of pentothal sodium.

The 1 case of death and the 7 instances of severe apnea reported here are attributable to errors of technic, but serve to emphasize how dangerous this complication may be.

From the viewpoint of the ophthalmic surgeon many of the postoperative sequelae of administration of pentothal sodium are extremely serious. Restlessness, nausea and vomiting are certainly dangerous when they follow an intraocular operation.

The rather frequent long periods of reaction which follow use of large amounts of pentothal sodium require the careful supervision of both the physician and the nurse so that prompt resuscitative measures can be taken when indicated.

University of Michigan Medical School.

CONGENITAL OPACITIES OF THE CORNEA

CAPTAIN FREDERICK H. THEODORE
MEDICAL CORPS, ARMY OF THE UNITED STATES

The question of congenital corneal opacities was one of the first to attract the attention of the older ophthalmologists. Controversial theories have been postulated as to the origin of such opacities, but none has been universally accepted. With the exception of perhaps one article, apparently no studies of this condition have appeared in the American literature.

The unusual opportunity offered me of examining 6 patients with this anomaly, 2 of them sisters, in whom the opacities were associated with anterior synechiae and other developmental defects, prompted this report, in the hope that it would throw additional light on a somewhat obscure subject.

REPORT OF CASES

Case 1.—Frances T., aged 6 years, was first seen by me on Feb. 7, 1942 at the Manhattan Eye, Ear and Throat Hospital, through permission of Dr. S. Falk. The ocular condition had been present since birth. Vision in the right eye was limited to light perception only and was unimproved with glasses; vision in the left eye was 20/20.

The right eye presented moderate ptosis, due to microphthalmos. Microcornea was also present, the cornea measuring 9 mm. in the vertical and 10 mm. in the horizontal diameter. The outstanding feature of the eye was the presence of a large, sector-shaped corneal opacity extending from the nasal limbus to a point 3 mm. from the temporal limbus and occupying the central 5 mm. of the cornea, completely obliterating the pupillary area (fig. 1). The opacity involved the posterior half of the cornea, fading in intensity anteriorly. The endothelial surface could not be studied. Attached to the margins of the opacity were a number of anterior synechiae, which consisted of thick, ropelike strands of iris tissue, originating mostly in the angle of the anterior chamber. A few strands came from the lesser circle. The iris itself was pale and had a vacuolated appearance, due to lack of most of its anterior, or mesodermal, tissue. The lens and the fundus could not be seen. Rotary nystagmus was present. The tension was 35 mm. (Schiøtz). The pupil dilated moderately.

Examination of the left eye revealed nothing abnormal except a thin, crescentic peripheral zone of superficial vascularization of the cornea from 8 to 1 o'clock and a persistent remnant of pupillary membrane. The tension was 35 mm. (Schiøtz).

Case 2.—Dorothy T., aged 11 years, the sister of the patient in case 1, was seen in the service of Dr. N. DeL. L. Fletcher, at the Manhattan Eye, Ear and Throat Hospital on Feb. 8, 1942. The ocular condition had been present since birth. Vision in her right eye was 20/30 — 1, and was unimproved with a + 0.50 D. sphere; vision in the left eye was limited to perception of hand movements. Exotropia of 45 degrees of arc was present in the left eye.

The left eye, which will be described first, presented a picture similar to and symmetric with that of the right eye of the patient's younger sister (case 1). The cornea was slightly microphthalmic, measuring 10 mm. in diameter. A tonguelike opacity arose at the limbus in the region from 9 to 12 o'clock and extended across the nasal two thirds of the cornea to obliterate the pupil likewise (fig. 2 *A*). This opacity, however, was less intense, involving chiefly the most posterior layers of the cornea, with little involvement of the stroma. The temporal border of the opacity was accentuated. Attached to it superiorly were four thick anterior synechiae, consisting of mesodermal elements of the iris arising from the angle of the anterior chamber, and attached inferiorly were several synechiae from the lesser circle of the iris. A few vessels invaded the corneal stroma at the base of the opacity. The lens, vitreous and fundus, which was seen with some difficulty, appeared normal.

The right eye presented a different type of abnormality. Microcornea was present, the cornea measuring 7.5 mm. in the vertical and 9 mm. in the horizontal diameter. The outstanding abnormality was an opacity which formed an almost complete ring around the peripheral 2 to 3 mm. of the cornea, extending from 4 to 3 o'clock (fig. 2 *B*). The major portion of the opacity, from 8 to 3 o'clock, appeared to consist chiefly of a flat membrane adherent to the posterior surface of the cornea. The membrane was seen to arise from the angle of the anterior chamber and was separate from the cornea inferiorly (from 4 to 8 o'clock), joining it only at its superior border by means of a heavy, irregular, knotty adhesion. Thus a free, troughlike interval, or space, was formed, the base of which was deep in the angle of the chamber (fig. 3). At the junction with the membrane the cornea was opaque in front and central to the line of adhesion. One strand of the membrane arose from the lesser circle.

The pupil was ectopic and dilated fairly well. The media and the fundus were normal.

The color of both irises was poor, owing to a paucity of mesodermal elements, which gave a vacuolated appearance. The tension was 23 mm. (Schiøtz) in each eye.

The mother and father of the patients in cases 1 and 2 presented no ocular abnormalities. The family history on both sides was negative for the defect. There was no consanguinity. The general physical examination of both patients revealed nothing abnormal. There was no syndactyly.

Presented in part at a meeting of the New York Academy of Medicine, Section of Ophthalmology, May 18, 1942.

From the Station Hospital, Miami Beach Training Base, Army Air Forces Technical Training Command, Miami Beach, Fla.

The following 4 cases were noted during processing examinations at Miami Beach, Fla., and are presented with the permission of Major Robert M. Johnson, Medical Corps, chief of the ophthalmic section, Station Hospital.

Case 3.—R. L., aged 21, a soldier, was seen at the Eye Clinic, Station Hospital, Miami Beach Training Base, on April 16, 1943. His ocular condition had been present since birth. Vision in the right eye was 20/30, and examination of this eye showed nothing abnormal.

Vision in the left eye was limited to perception of hand movements and could not be improved with a correction of + 3.00 D. sph. ⊃ + 2.00 D. cyl., axis 80. The eye showed slight microphthalmos, as well as a small cornea, which measured 10.5 mm. in each diameter. Slight ptosis was present. The tension was 18 mm. (Schiøtz).

The cornea presented a large central, roughly circular opacity, measuring about 5.5 mm. in diameter (fig. 4). The opacity was most intense posteriorly but involved in diminishing degree the entire stroma up to Bowman's membrane. The endothelium was disorganized, and

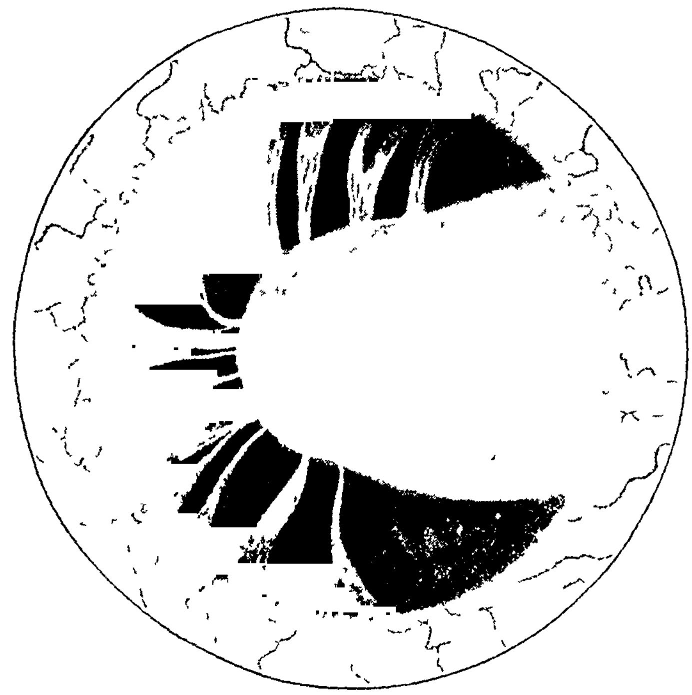

Fig. 1 (case 1).—Right eye.

whorllike defects in it could be seen. In two places in the inferior portion of the opacity thick, broad strands of synechiae arising from the lesser circle of the iris were attached to the posterior corneal surface by means of heavy adhesions. Large defects in the structure of the anterior portion of the iris were present in its inferior half, giving a vacuolated appearance. The pupil dilated fairly well. Examination of the lens revealed a congenital anterior capsular cataract and a small opacity involving the embryonic nucleus and the posterior Y-shaped suture.

The family history was without significance except that an aunt had had congenital cataracts.

Case 4—D. A., aged 19, a soldier, was seen at the Eye Clinic, Station Hospital, Miami Beach Training Base, on May 8, 1943. His ocular condition had existed since birth. Vision in the right eye was 20/50 and with a —0.50 D. sphere it was improved to 20/40. Vision in the left eye was 20/40 and was improved to 20/30 by a similar correction. A slight degree of microcornea was present in each eye.

Both eyes presented a similar and almost symmetric picture (fig. 5). In the right eye a corneal opacity, measuring 2 by 3 mm., was present midway between the limbus and the center of the cornea at 3 o'clock. The opacity was most intense posteriorly, where in its center a number of anterior synechiae, arising in broad bands chiefly from the lesser circle of the iris, formed a dense attachment. Around and anterior to this the opacity gradually faded out, but almost reached Bowman's membrane. The iris was thin and lacking in mesodermal elements in its nasal half. Congenital

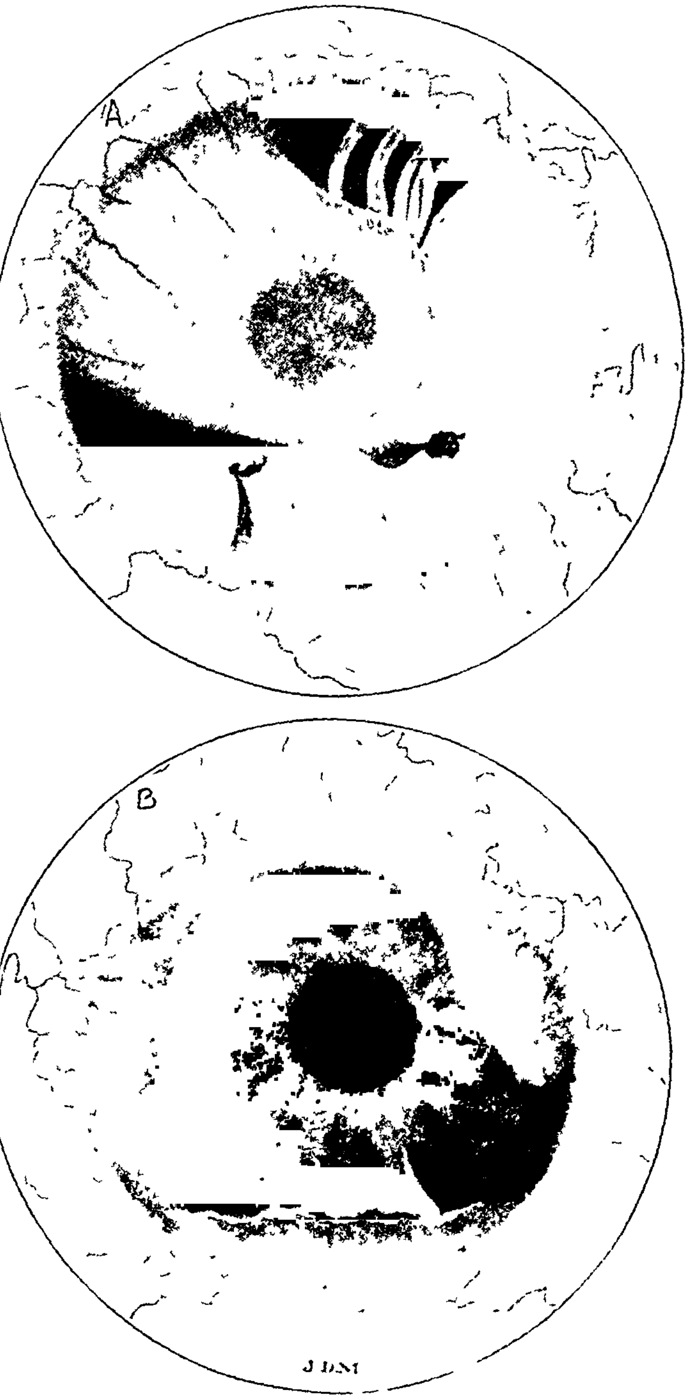

Fig. 2 (case 2).—*A*, left eye; *B*, right eye.

pigment was noted on the anterior capsule of the lens, as well as a fine strand of persistent pupillary membrane.

In the left eye an opacity, similar in every detail, to which similar anterior synechiae were attached, was present at 9 o'clock, midway between the limbus and the center of the cornea. The pupil was piriform, with the long diameter horizontal. Congenital pigment was observed on the capsule of the lens. The tension was normal. The family history was without significance.

Case 5—E. G. S., a soldier aged 2[illegible], was seen at the Eye Clinic, Station Hospital, Miami Beach Training Base, on May 18, 1943. The ocular condition had

been present since birth. Vision in the right eye was 20/160 and was improved to 20/80 with a correction of — 2.00 D. sph. ⊂ + 3.25 D. cyl., axis 90. Vision in the left eye was 20/80 and was improved to 20/40 with a correction of + 2.00 D. cyl., axis 5. The tension was normal in both eyes.

Both eyes presented a condition similar to that of the right eye in case 2. In each eye a flat, ringlike membrane, apparently arising from the angle of the anterior chamber, was attached at its central edge by means of a thick, irregular adhesion to the peripheral 2 to 3 mm. of the cornea from 3 to 9 o'clock (fig. 6). Peripherally, as in case 2, a small free, or troughlike, interval between the membrane and the cornea was seen in places. The corneal stroma anterior to it showed some relucence posteriorly.

The pupil of the right eye was elliptic and was situated so far temporally as to preclude useful vision in this eye. In both eyes the color of the iris was a dirty, muddy gray, due to absence of the anterior layers

Fig. 3 (case 2).—Slit lamp view of the inferior portion of the cornea of the right eye.

of the iris. In the lens of the left eye a fine reduplication cataract and a partial lamellar cataract were noted. The family history was without significance

Case 6.—D. T., a soldier, was seen at the Eye Clinic, Station Hospital, Miami Beach Training Base, on March 26, 1943. The condition in his left eye had been present since birth.

Examination revealed that the right eye was normal, with visual acuity of 20/20.

The left eye had no light perception and was microphthalmic. The palpebral fissure of this eye was 2.5 mm. narrower than that of the right eye. Microcornea was also present, the vertical diameter being 8.75 mm. and the horizontal diameter 9.5 mm.

The left eye presented several anomalous features (fig. 7). First, the superior temporal quadrant of the cornea was the site of a fine relucence of the posterior layers, culminating in a more intense, small opacity at the apex of the quadrant near the center of the cornea. Several thick bundles of iris tissue formed anterior synechial attachments to the main posterior opacity, and at 3 o'clock a synechia, arising from the lesser circle of the iris, formed part of the opacity's sharp inferior margin. Over the entire extensive area no normal endothelium was seen

The second feature of note was the absence of the lens. In its place appeared to be a pseudogliomatous mass, which in the main consisted of a gray-brown tissue, rimmed nasally by a border of white, which was adherent to the ciliary processes. The latter were seen nasally. The eye could not be transilluminated, an

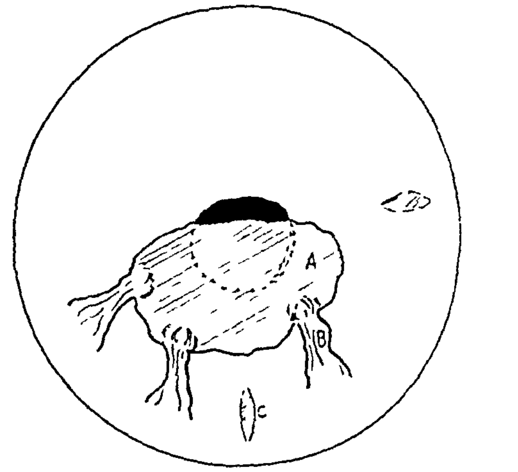

Fig. 4 (case 3).—Diagrammatic sketch of the left eye. *A* indicates a corneal opacity; *B*, an anterior synechia, and *C*, a stromal defect in the iris.

indication of the extent of the process. The mass was in no place adherent to the cornea. No evidence of old inflammation was noted.

Here, too, no family history of a similar defect was obtained. A questionable story of injury at birth was given.

Six cases are presented in which the patients were born with opacities involving chiefly the deeper layers of the cornea to which anterior synechiae were attached. The opacities were of two types: one of greater density generally located either centrally or somewhat off center, and the other consisting of a peripheral membrane arising

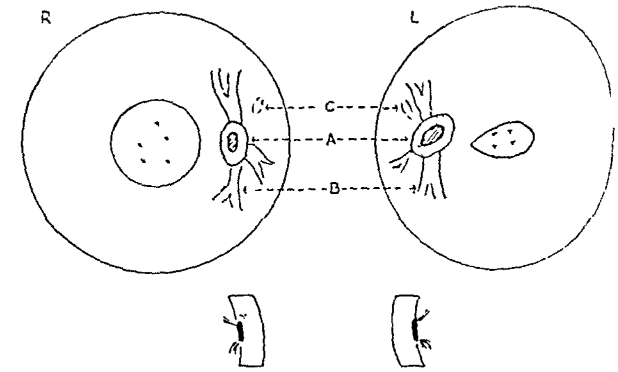

Fig. 5 (case 4).—Diagrammatic sketch of both eyes. *R* indicates the right eye; *L*, the left eye; *A*, a corneal opacity; *B*, an anterior synechia, and *C*, a stromal defect in the iris.

from tissue in the angle of the anterior chamber. As was to be expected, the central opacities produced impaired vision; the peripheral opacities did not. In no case was there evidence of inflammation. A familial incidence was present in 2

ases, as sisters were involved. In 1 of these 2 ases (case 2) both kinds of opacities occurred, he type differing in the two eyes. In case 4 bilateral symmetric opacities of the central, or first, ype were seen, and in case 5, similarly distributed opacities of the peripheral type were noted. In case 6 the condition was complicated by the absence of the lens and the presence of pseudogliomatous tissue.

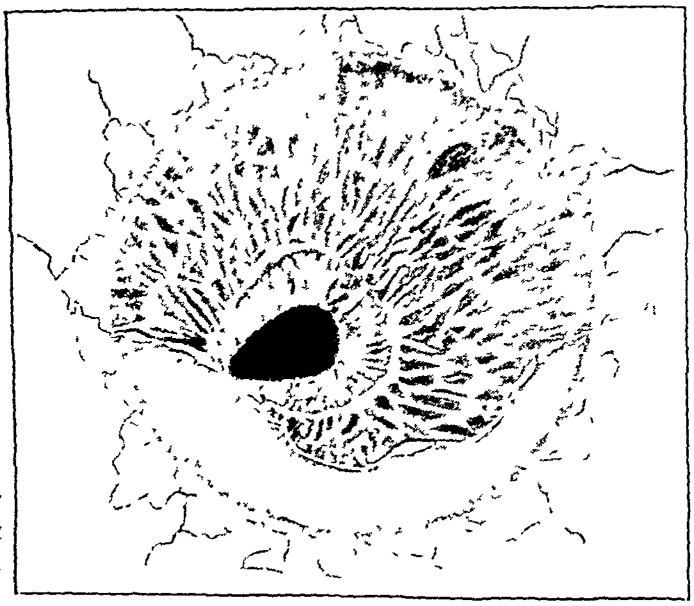

Fig. 6 (case 5).—Right eye. Drawing by Captain William H. Bonser, Medical Corps, Army of the United States.

The anterior synechiae arose for the most part from the angle of the anterior chamber, although some originated from the lesser circle of the iris. In every case, especially in the area corresponding to the corneal involvement, hypoplasia of the anterior, or mesodermal, layers of the iris was apparent. Marked corectopia was noted in the right eye in case 4 and dyscoria in the left eye in case 5.

In 3 instances (cases 1, 3 and 6) microphthalmos was present.

In view of the controversy concerning the origin of corneal opacities, these cases are of significance.

REVIEW OF LITERATURE

A review of the entire literature on corneal opacities with anterior synechiae is neither necessary nor feasible. Most of the important contributions, however, have been consulted.

It was natural for the earlier authors to attribute the condition to the end results of an external inflammatory process, notably ophthalmia neonatorum with perforation of the cornea. Ballantyne [1] mentioned cases described by von Beck in 1838, Samelsohn in 1880, Wintersteiner in 1893 and van Duyse in 1902 as illustrations of this point of view. While it is possible that the lesion might sometimes arise in this manner, such a theory can be considered tenable only in special instances.

At one time the theory that the abnormality was due to intrauterine inflammation had a considerable number of adherents. Perhaps the most outstanding proponent of this theory was von Hippel,[2] who termed the condition "internal ulcer of the cornea." Another protagonist was Ballantyne,[1] who published an extensive review in 1905. The basis of the theory was the observation of what appeared to be microscopic evidence of an old inflammatory process. It is probable that some cases do fall into this category, but, with increasing knowledge, it became evident that the presence of inflammation during fetal life could not explain the anomaly in most cases, as inflammatory signs were absent. Furthermore, the theory could not explain the hereditary tendency, the symmetry and bilaterality of the defect and the association with congenital anomalies of other parts of the body, as well as of the eye.

The only explanation left, therefore, was that corneal opacities with anterior synechiae, present from birth, arose as developmental defects. Among the most ardent advocates of this theory was Collins,[3] who, on the basis of clinical and pathologic studies, concluded that the cause lay in faulty development of the mesoderm that

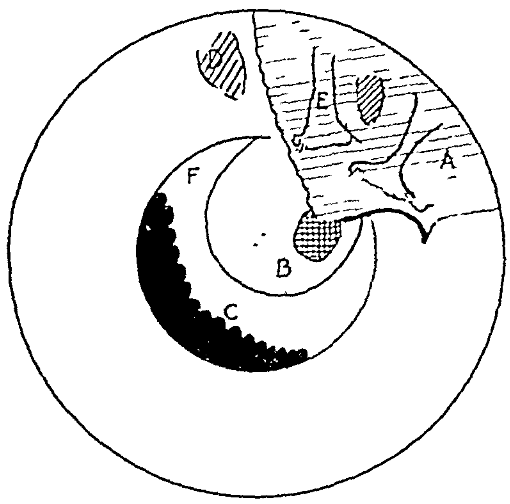

Fig. 7 (case 6).—Diagrammatic sketch of the left eye. *A* indicates a deep corneal opacity; *B*, the pigmented portion of the pseudogliomatous mass; *C*, the ciliary processes; *D*, the stromal defect in the iris; *E*, anterior synechia, and *F*, the white portion of the pseudogliomatous mass.

1. Ballantyne, A. J.: Synechiae of the Iris and Pupillary Membrane, Tr. Ophth. Soc. U. Kingdom 25:[illegible]

2. von Hippel, cited by Duke-Elder,[1] p. 1282.

3. Collins, E. T.: Lectures on the Anatomy and Pathology of the Eye. Lecture III, Lancet 2:1463, 1894; Adhesion of a Persistent Pupillary Membrane to the Cornea in the Eye of a Cat, Tr. Ophth. Soc. U. Kingdom 27:2[illegible], 1907; C[illegible] 29:1[illegible]

grows in to form most of the cornea, including the endothelium and Descemet's membrane, the anterior chamber, the anterior portion and stroma of the iris and the trabecula. Collins expressed the belief that in most cases the defect was due to partial failure in formation of Descemet's membrane, with adhesion of the iris to the defective area. He postulated that congenital anterior staphyloma was due to complete failure of Descemet's membrane to appear, while he explained anterior synechia without opacifications as the result of failure of a small area of endothelium to differentiate in the presence of normal development of Descemet's membrane. Mayou [4] came to a similar conclusion.

In addition, Collins [5] reported the cases of 2 sisters in which bilateral corneal opacities were of such density as to obscure the irises. Moxon [6] also described congenital opacities in 2 sisters, but the irises were normal.

Important confirmation of the work of Collins was afforded by Seefelder,[7] who concluded that a developmental defect in Descemet's membrane occurs first and that adhesions are the result possibly of compression of the ingrowing pupillary membrane.

A different theory, based also on the concept of a developmental aberration, was advanced by Peters,[8] who called attention to the central location of the corneal defect and expressed the belief that the anomaly resulted from faulty separation of the lens vesicle from the surface ectoderm. He expressed the opinion that the ingrowing mesoderm was poorly developed and unable effectively to produce separation of the lens from the cornea. It is a criticism of Peters' theory that the lens usually reveals no important abnormalities, but Hoffmann [9] described a case that appeared to offer perfect corroboration of Peters' explanation. In each eye in this case the lens was luxated and was adherent to the back of the cornea at the site of a deep central opacity. In addition, a coloboma of the iris was present in each eye.

Berliner [10] described the cases of 2 cousins in which a so-called hyaline membrane on the posterior corneal surface, to which anterior synechiae were attached, was associated with syndactyly and microphthalmos. He expressed the belief that these cases were related to others previously reported by Ciotola,[11] who had studied the association of microphthalmos with other abnormalities of the body, as well as of the eye, and had asserted that such a clinical picture constitutes a definite syndrome. Berliner was chiefly concerned with this phase of the subject, but concluded that the lesion in his cases was unquestionably of congenital origin.

COMMENT

The 6 cases reported in this paper are interesting from several points of view. First, it is worth while merely to point out that corneal opacities with anterior synechiae may occur as a congenital anomaly, as many clinicians who first encounter such a lesion are likely to consider the aftermath of an inflammatory process. It should also be mentioned that the anomaly, while not exceedingly rare, is not frequent, inasmuch as the 4 cases at Miami Beach Training Base were encountered during the examination of hundreds of thousands of men. In 2 other cases the condition appeared to have a similar origin, but as the picture was not clearcut, the cases were not included in the report.

There can hardly be any doubt that the lesions in the cases presented in this paper arose from a developmental defect. Only in case 6 can any question be raised. In no instance was any evidence of inflammation present. In all cases the condition had been noted from birth. In cases 1 and 2, in which the lesions occurred in sisters, a familial tendency was indicated; in cases 2, [illegible] and 5 there was bilateral involvement, and in the last 2 cases a pronounced symmetry was evident. Microphthalmos, another congenital condition, was present in cases 1, 3 and 6. All these points suggest the congenital nature of the condition.

The cases are also significant because they offer additional confirmation of the theories of Collins and of Seefelder. One could hardly expect better clinical examples of the anomaly than the right eye in case 2 and both eyes in case 5, ...

4. Mayou, M. C.: A Case of Congenital Synechiae with Buphthalmos (Anterior Staphyloma), Tr. Ophth. Soc. U. Kingdom **30**:120, 1910.

5. Collins, E. T.: Two Children in the Same Family with Congenital Opacities of Both Corneae, Tr. Ophth. Soc. U. Kingdom **30**:120, 1910.

6. Moxon, F.: Congenital Diffuse Non-Inflammatory Corneal Opacities in Two Sisters, Brit. J. Child. Dis. **2**:257, 1914.

7. Seefelder, R.: Pathologisch-anatomische Beiträge zur Frage der angeborenen zentralen Defektbildung der Hornhaut-Hinterfläche, Klin. Monatsbl. f. Augenh. **65**:539, 1920.

8. Peters, A.: Ueber angeborene Defektbildung der Descemetschen Membran, Klin. Monatsbl. f. Augenh. **1**: 27 and 105, 1906; Zur Frage der angeborenen Trübungen und Staphylome der Hornhaut, ibid. **70**:629, 1923.

9. Hoffmann, R.: Zur Entwicklungsweise der angeborenen Hornhaut-trübungen, Arch. f. Augenh. **105**: 162, 1932.

10. Berliner, M. L.: Unilateral Microphthalmia with Congenital Anterior Synechiae and Syndactyly, Arch. Ophth. **26**:653 (Oct.) 1941.

11. Ciotola, G.: Microftalmo e malformazione delle dita (sindattilia, polidattilia), Boll. d'ocul. **17**:855, 1938.

which the opacification was entirely peripheral. Moreover, in all but 2 of the cases the opacity, even if of the central type, began at the limbus. Again, for the most part the anterior synechiae arose peripherally, from deep in the angle of the anterior chamber. If the developmental fault lies with the mesoderm, which grows in from the periphery, the aforementioned abnormalities might readily occur. Moreover, the hypoplasia of the anterior layers of the iris, seen in all the cases; the corectopia, noted in case 5, and the dyscoria, observed in case 4, point to other mesodermal anomalies. Only in case 3, in which a fine anterior capsular cataract was noted, was there any special confirmation of Peters' theory.

Case 6 presents a somewhat more complicated problem. The corneal opacity, the anterior synechiae and the microphthalmos all point to a developmental aberration; yet one hesitates to place the absence of the lens on a congenital basis. True congenital aphakia is exceedingly rare and, as Duke-Elder [12] stated, tends to be associated with microphthalmos, as well as defects of the anterior segment. This author, however, mentioned several cases of aphakia without much deformity and credited Mann with a case of this condition in a fetus in which the cornea was only slightly thickened. Other explanations, aside from the obvious one of extrusion of the lens after trauma, include absorption of a congenital cataract, as recorded by Duke-Elder,[13] and absorption of the lens as a result of intrauterine inflammation. Either of the latter two mechanisms, as well as true congenital aphakia, may have occurred in case 6. The pseudogliomatous mass present in this case may have been the end result of such an inflammatory process, but in the absence of gross evidence it might better be considered of developmental origin.

12. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1346.

13. Duke-Elder,[12] p. 1374.

SUMMARY

Corneal opacities with anterior synechiae, 6 cases of which are reported, are of two types: one central and the other of peripheral origin. In 3 cases microphthalmos was present. In 1 case aphakia was also noted. In each case the condition had been present since birth.

Various theories as to the origin of the condition have been advanced. Its occurrence as a congenital anomaly due to faulty development of the ingrowing mesoderm that forms the corneal stroma, the endothelium, Descemet's membrane, the anterior layers of the iris and the trabecula is believed to be the most likely explanation of the condition. The cases reported appear to support this concept.

Another developmental theory ascribes the defect to incomplete separation of the lens vesicle from the surface ectoderm. A case cited bears out this belief. Other explanations base the defect on an inflammatory process, either intrauterine or postnatal.

It is believed that while all the theories are probably applicable in certain cases, the condition is due for the most part to a developmental anomaly of the mesoderm.

JUVENILE MACULAR EXUDATIVE CHOROIDITIS

JUVENILE DISCIFORM DEGENERATION OF THE MACULA (JUNIUS)

FRANCIS H. ADLER, M.D., AND HUNTER SCARLETT, M.D.

PHILADELPHIA

This is a report of 3 cases of macular disease which we believe most nearly fall under the diagnostic entity called juvenile macular exudative choroiditis, or juvenile disciform macular degeneration, described by Junius in 1930.[1] Because of the ease with which the disease may be mistaken for early malignant melanoma, the differential diagnosis of this condition is of some importance.

All the patients were young, healthy adults, in whose condition neither trauma nor any antecedent illness seemed to play a part. Their uniform complaint was a rather gradual depreciation of central vision in one eye only, which progressed within a matter of weeks until visual acuity was approximately 6/100, with an absolute central scotoma corresponding in size and shape to the ophthalmoscopically visible lesion in the macula.

The lesions when first seen were approximately the same in 2 cases. In the third case the lesion was older and was evidently undergoing absorption. The area in each case was somewhat oval, well circumscribed and pigmented and in places seemed to be covered with connective tissue. The color was not uniform throughout, but in some places was light gray and in others rather dark. Around the edges were a number of small hemorrhages, which seemed to come from under the pigmented mass. No difference in level could be made out between the mass and the surrounding retina, although the impression was that the mass was slightly elevated.

During the period of observation the only perceptible changes were the absorption of some of the hemorrhages and the appearance of fresh ones, always at the edge of the lesion. The pigmented mass itself changed somewhat; from time to time it seemed as though the amount of pigment shifted in a given area, and in 1 case the central pigment disappeared almost entirely. At no time was there any evidence of inflammation in the eye. There was no conjunctival or ciliary flush; no deposits on the posterior surface of the cornea; no floaters, or even a flare in the aqueous; no cellular debris in the retrolental space, and no opacities in the vitreous. About the lesion itself there was no edema or exudative reaction such as one is accustomed to associate with true inflammatory lesions of the choroid. The eyeground presented no other lesions, of either present or past origin. The fellow eye was healthy in all cases. Except for a central scotoma, the fields were normal.

During a period of observation of six months to a year there was gradual but definite improvement of vision to 6/40 in 2 cases and to 6/12 in 1 case.

REPORT OF CASES

CASE 1.—H. M. W., a man aged 35, was referred to Dr. Norman L. Cutler, of Wilmington, Del., who had had him under observation since October 1941. At that time the patient had consulted Dr. Cutler for failing vision in the right eye for the preceding three weeks. His visual acuity, however, was then nearly 20/3[illegible]. Within a week vision in the right eye had decreased to 20/70. When we first saw him it was 20/300. Vision in the left eye was 20/20, and this eye was entirely normal.

On external examination both eyes appeared normal. Examination of the anterior segment of the right eye with the slit lamp showed no evidence of inflammation. Ophthalmoscopic inspection of this eye showed that the media were clear. The disk was oval, of good color and well outlined. In the macula was a pear-shaped area, which was oval in the horizontal diameter, deeply pigmented and surrounded by deep hemorrhages. This area seemed to be raised, and the blood vessels coursed over it. There was no edema around it, and the rest of the fundus was normal.

Complete physical examination revealed nothing abnormal, and studies for foci of infection gave negative results. There was no history of injury, and no member of his family or any of his forebears, as far as he knew, had had any similar ocular trouble. The only positive observation was a *mild* degree of allergy to tuberculoprotein.

Since August 1942 there has been little change in the lesion. Some of the original hemorrhages have disappeared, and fresh ones have been noted from time to time. The central scotoma, which was present on the first examination, has decreased in size, and vision has improved from 20/300 to 20/100. At no time has there been any evidence of inflammation.

Figure 1 *A* shows the condition of the right eye in January 1943, and *B*, the appearance of the same eye in June 1943.

CASE 2.—Ensign W. J. P., a man aged 27, first noticed diminution of vision in the left eye in the latter part of December 1942. He had been present at the bombing

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From the Department of Ophthalmology of the University of Pennsylvania.

Read at a meeting of the College of Physicians of Philadelphia, Section on Ophthalmology, April 15, 1943.

1. Junius, P.: Ztschr. f. Augenh. **70**:129, 1930.

of Pearl Harbor but was emphatic in his statement that he was nowhere near any explosions which could have affected him, even from blast. He had been seen by numerous Navy physicians and had finally been given permission to get civilian medical advice.

The right eye was entirely normal, with visual acuity of 20/20. Vision in the left eye was 20/300. The left eye was normal in every respect save for a pigmented lesion, oval and well circumscribed, in the macula, which was surrounded by several small hemorrhages. At first the lesion seemed elevated, and there was some

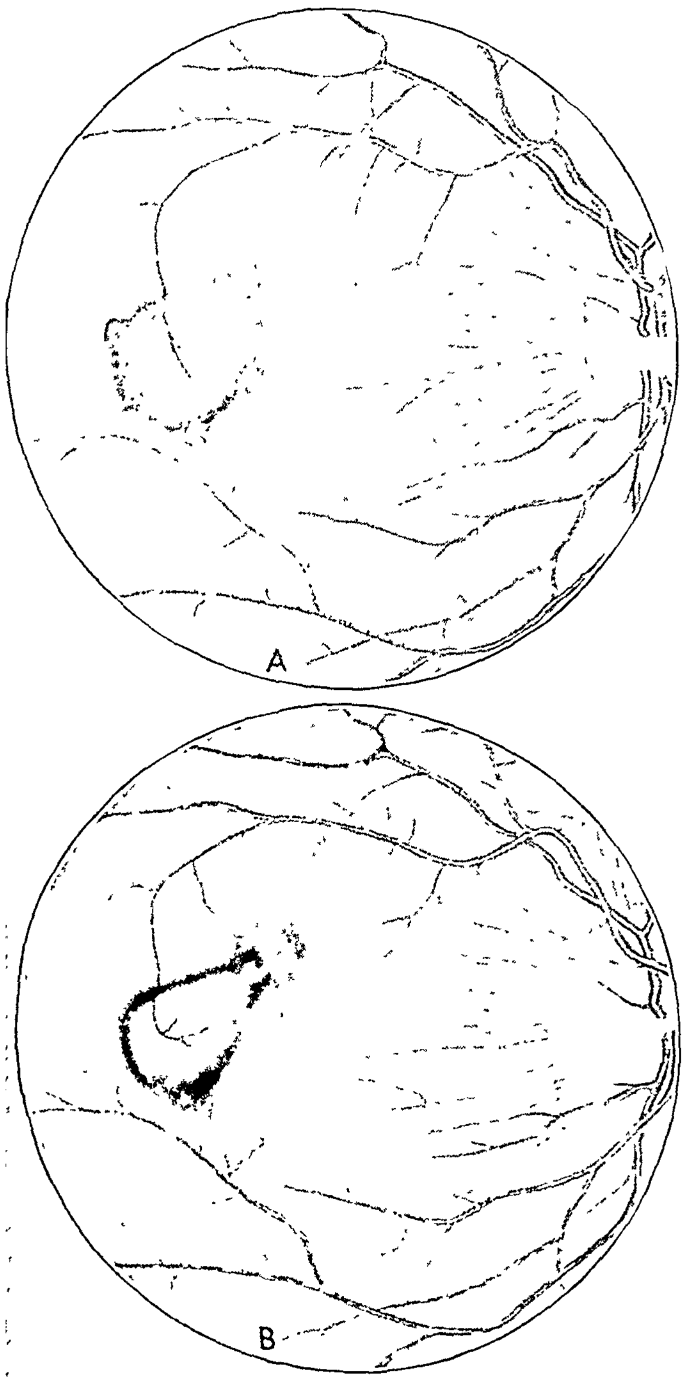

Fig. 1 (case 1).—*A*, condition of the right eye in January 1943; vision 20/300.

B, condition of the same eye in June 1943. The lesion itself was smaller, but there were numerous thin hemorrhages over the entire nasal side of the lesion, while those on the temporal side had disappeared. Vision was 20/100.

question whether it might not be an early melanoma. The tension was 17 mm. in each eye and remained at about this level. No signs of inflammation were ever noted. Vision in the left eye gradually improved to 20/120, and the central scotoma was slightly smaller at the time of the last examination than it was at the first observation.

The history and the physical examination revealed nothing significant. All tests failed to show any possible cause of the lesion. The patient seemed to be exceptionally healthy. He has recently been given an honorable discharge from the Navy and was last seen on April 15, 1943.

Figure 2 shows the appearance of the lesion on Oct. 7, 1942.

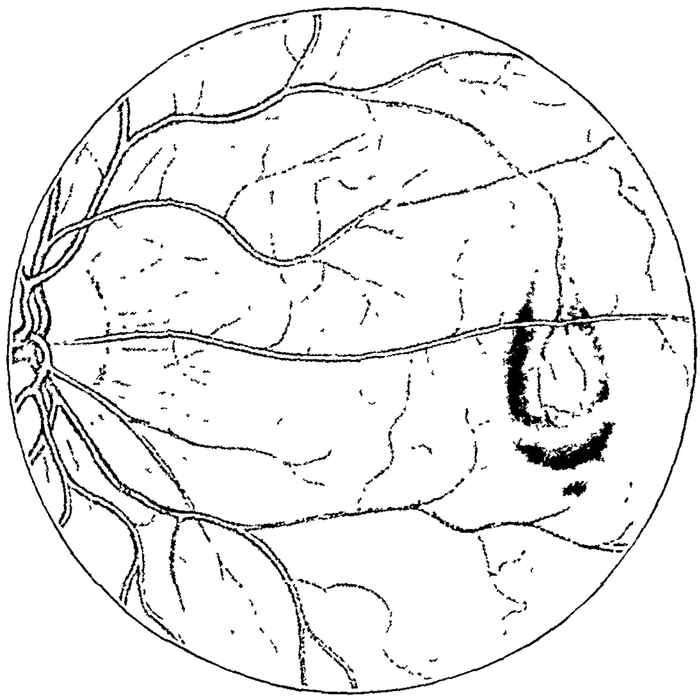

Fig. 2 (case 2).—Condition of the fundus of the left eye in October 1942; vision 20/300. Note the small, discrete hemorrhage below the lesion and the faint one adjacent to and on the temporal side of the lesion.

Case 3.—M. L., a woman aged 30, noticed blurring of vision in the right eye on Christmas eve 1942. She was examined by several physicians and was seen by

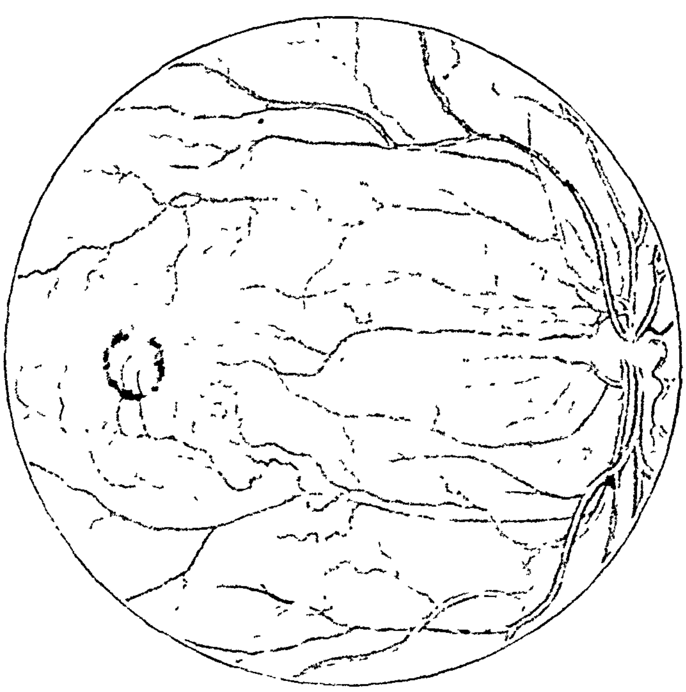

Fig. 3 (case 3).—Condition of the right eye in April 1943; vision 20/27.

one of us (F. H. A.) in consultation with Dr. Harold Scheie, by whose permission we report her case.

On first observation vision was 20/50 in the right eye and 20/25 in the left, or normal, eye. The right eye was normal save for a macular lesion, which appeared to be in a later stage of disciform degeneration than

the lesions in the preceding 2 cases. In addition to the macular lesion, numerous yellowish, discrete areas, which looked like drusen, were scattered through the fundus of each eye. No inflammatory signs were present in either eye during our period of observation. A very small paracentral scotoma was present.

The lesion in this case had much less pigment than the lesions in the preceding 2 cases, and no hemorrhages were present. We cannot be sure that this case really belongs in this category, for physicians who had previously seen the patient stated that the area was one of subsiding choroiditis and that edema of the retina still persisted. When we saw her, however, no inflammatory signs were present, and the condition resembled disciform degeneration more than an old inflammatory lesion. Vision when she was last seen, on April 20, 1943, was 20/27 in the diseased eye. Figure 3 shows the appearance of the lesion on that date.

DIFFERENTIAL DIAGNOSIS

We shall consider the following diagnostic possibilities: (1) acute macular choroiditis, or central choroiditis; (2) tuberculosis of the macula and benign lymphogranuloma; (3) choroidal and subchoroidal hemorrhage in the macula; (4) nevus and malignant melanoma; (5) heredodegeneration and familial degeneration of the macula, and (6) juvenile macular exudative retinitis, or juvenile disciform degeneration.

Acute Macular Choroiditis.—Acute macular choroiditis has all the characteristics of similar isolated lesions in the other regions of the eyeground, but because of the anatomic peculiarities, the lesion is likely to be large and single. The lesion is highly exudative and invariably shows deposits on the corneal endothelium, floaters in the aqueous and opacities in the vitreous. In the early stages the lesions are nonpigmented and the retina is edematous. When the stage of atrophy begins, there is loss of the substance of the retina with exposure of the choroidal blood vessels, or of the bare sclera, and the pigment is nearly always distributed at the edges of the lesion, and not in the center.

It is true that Hepburn [2] pointed out that in the type of choroiditis which he designated as superficial, in contrast to the deep variety, there is often considerable proliferation of pigment over the surface of the patch, with heaping up of black masses, most of the pigment being retinal. Further, he stated that in this type there are less likely to be inflammatory signs, such as opacities in the vitreous, pain and sudden onset of visual loss—the condition coming on gradually and without any symptoms except for visual deterioration.

Hemorrhages are seldom seen in association with acute macular choroiditis and do not keep recurring when they are present. Once the lesion has fully formed, vision in that area is irretrievably lost.

Tuberculous Macular Choroiditis and Similar Lesions Due to Benign Lymphogranuloma.—The diagnosis of all tuberculous lesions of the uveal tract must be presumptive and is based on the ophthalmoscopic appearance of the lesion, its clinical course and the patient's degree of allergy to tuberculoprotein. This is also true of lesions supposedly due to sarcoid. All these lesions are highly exudative and so do not resemble the condition under discussion.

Choroidal and Subchoroidal Hemorrhage in the Macula.—Bedell [3] collected a large number of cases of choroidal hemorrhage in various regions of the fundus. Aside from cases of traumatic expulsive choroidal hemorrhage, which has nothing to do with the condition under discussion, he reported a number of cases of choroidal hemorrhages occurring in the macula. In some of these cases absorption of the blood was followed by abnormal pigmentation, often accompanied by a gray-white, closely adherent membrane, similar in appearance to the sheet of tissue in retinitis proliferans. In cases in which the blood was subchoroidal, Bedell claimed it could be differentiated from pigment by the latter's being darker, more homogeneous and more irregular in outline, with no great variations from time to time. Under the heading of choroidal hemorrhage Bedell included cases of senile macular degeneration, which, he asserted is really choroidal hemorrhage in the later stages when the blood is no longer visible as such. Moore [4] reported the case of a man aged 46 with a subchoroidal hemorrhage which contained some pigment, but the hemorrhage was massive and could not have been mistaken for anything else.

Heredodegeneration and Familial Degeneration of the Macula.—Many forms of so-called heredodegeneration and familial degeneration of the macula are described in the literature. There is no constancy in the ophthalmoscopic appearance of the macular lesions, and the diagnosis cannot be made from the fundic picture itself but is based entirely on a family history that more than one member of the same family is similarly affected.

Heredodegeneration affects several generations, while with the familial type only the members of one generation have the disease, and the condition is not transmitted necessarily to the offspring. In none of our cases could it be

2. Hepburn, M. L.: Tr. Ophth. Soc. U. Kingdom **32**:361, 1911-1912.

3. Bedell, A. J.: Signfiicance of Choroidal Hemorrhage, Arch. Ophth. **8**:186 (Aug.) 1932.

4. Moore, F.: Tr. Ophth. Soc. U. Kingdom **30**:16[illegible], 1910.

arned that any other member of the family as similarly affected.

Nevus and Malignant Melanoma.—Choroidal vus may occur in the region of the macula and round, bluish or slate gray and usually slightly naller than the disk. No hemorrhage or interrence with visual acuity is present in cases of vus. The lesion is congenital and usually does t change, although at any time it may begin grow and become malignant.

The typical circumscribed malignant melanoma the choroid is a small, lenticular or elliptic gmented mass when it is first discovered; it ay occupy any position in the fundus, although is not common directly in the macula. Hemorage is not usual in the early stages but may be en, and the presence of blood is not a sign at the lesion is not a melanoma. Further, flammatory signs are frequent in the tumor, though this fact is not stressed in most textoks. In fact, most texts deal almost entirely th the histologic appearance of this lesion and ve little to say regarding its early appearance. s a result, a diagnosis of malignant melanoma usually not made in regions like the macula, here transillumination is impossible until the mor has attained considerable size and by growth has shown its true nature.

Juvenile Macular Exudative Choroiditis, or uvenile Disciform Degeneration of the Macula. -Junius was the first to describe this condition a clinical entity. He stated that it was related , but not identical with, the condition called 'elapsing central retinitis" by von Graefe. The sease is characterized by the following features:

1. A slowly developing macular lesion, usually nilateral, in a young adult, with no history of auma or antecedent disease.

2. A circumscribed lesion, usually lenticular disklike, and containing considerable pigment arly in the development of the lesion.

3. The absence of acute inflammatory signs.

4. The presence of hemorrhages surrounding ie pigmented lesion and seeming to come from eneath it.

5. Gradual improvement in visual acuity. The ision may not return to normal, but usually nproves to about 6/40.

Bailliart[5] reported a case of the disease in a woman of 25 in which the lesions were bilateral. In each macula was a lesion resembling a pigmented cyst, over the anterior surface of which the macular vessels passed. The cyst seemed to disappear, and the lesion then resembled a hole in the macula. The evolution of the condition in this case took less than three months, after which vision tended to improve. The illustrations which accompany Bailliart's case more nearly resemble the appearance of the lesions in our cases than any others we have found in the literature.

Wilmer[6] illustrated the early and late stages in 2 of his cases. His figures show a much more diffuse macular lesion than was present in our cases.

Few cases of this disease have been reported, probably because the condition has been regarded as ordinary macular choroiditis. The lesion is not common, of course—in fact, much less so than the similar lesion in older people, called senile disciform degeneration (Junius and Kuhnt). The cause of both the juvenile and the senile type of disciform degeneration differs from that of the highly exudative macular choroiditis and should be differentiated from it. Both forms of disciform degeneration are probably due to choroidal or subchoroidal hemorrhage, although the evidence for this in the case of the senile type is scant (Verhoeff and Grossman[7]) and the literature holds no evidence of this origin for the juvenile type, since none of the recognized cases of the disease were studied histologically.

SUMMARY

A condition with the characteristics of juvenile disciform degeneration of the macula, described first by Junius as juvenile macular exudative choroiditis, may be easily mistaken for an early malignant melanoma of the choroid. Recognition of this condition is therefore important.

Hospital of the University of Pennsylvania.

5. Bailliart, P., and others: Traité d'ophtalmologie, Paris, Masson & Cie, 1939, vol. 5, p. 386.

6. Wilmer, W. H.: Atlas Fundus Oculi, New York, The Macmillan Company, 1934.

7. Verhoeff, F. H., and Grossman, H. P.: Pathogenesis of Disciform Degeneration of Macula, Arch. Ophth. **18**:561 (Oct.) 1937.

EXPERIMENTAL STUDIES ON FATIGUE OF ACCOMMODATION

I. PLAN OF RESEARCH AND OBSERVATIONS ON RECESSION OF NEAR POINT OF ACCOMMODATION FOLLOWING A PERIOD OF INTERPOLATED WORK ON THE OPHTHALMIC ERGOGRAPH

CONRAD BERENS, M.D.
AND
SAUL B. SELLS, Ph.D.
NEW YORK

The mechanism of accommodation has been the subject of much study and of much controversy. There is no agreement yet as to the exact mechanism of accommodation. There is evidence, however, that accommodation is subject to fatigue, i. e., decrease of power to accommodate resulting from prolonged exercise. Some authorities regard fatigue of the accommodative neuromuscular system as the central factor in the mechanism of ocular fatigue.

Positive results with respect to fatigue of accommodation have been reported by a number of investigators. Berens and Stark [1] reviewed the literature up to 1932. They discussed the positive findings of Ferree,[2] Lancaster and Williams [3] and Howe [4] and the work of Berens and his associates from 1918 on.[5]

Ferree,[2] using a method which consisted in observing the letters "li" on a white card set at a distance within the punctum remotum for a period of three minutes, recorded during this time the intervals of blurred and cleared vision. This test was given before and after periods of ocular work, and the two sets of results were compared. Ferree maintained that increase in the time that the test object was blurred after use of the eyes was the result almost entirely of changes in muscular control of the refracting mechanism. His explanation of these observations was

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From the Department of Ophthalmology, New York University.

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1. Berens, C., and Stark, E. K.: (*a*) Studies in Ocular Fatigue: III. Fatigue of Accommodation; History, Apparatus, and Methods of Graphic Study, Am. J. Ophth. **15**:216, 1932; (*b*) Studies in Ocular Fatigue: IV. Fatigue of Accommodation; Experimental and Clinical Observations, ibid. **15**:527, 1932.

2. Ferree, C. E.: Tests for the Efficiency of the Eye Under Different Systems of Illumination and a Preliminary Study of the Causes of Discomfort, Tr. Illum. Engin. Soc. **8**:40 (Jan.) 1913.

3. Lancaster, W. B., and Williams, E. R.: New Light on the Theory of Accommodation with Practical Applications, Tr. Am. Acad. Ophth. **19**:170, 1914.

4. Howe, L.: Measurement of Fatigue of the Ocular Muscles, Tr. Sect. Ophth., A. M. A., 1912, p. 423; The Fatigue of Accommodation, as Registered by the Ergograph, J. A. M. A. **67**:100 (July 8) 1916; Varieties of Fatigue as Registered by Ergograph, Tr. Ophth. Soc. **15**: 145, 1917.

5. Berens, C.: The Manual of the Ophthalmologic Department, in Manual of the Medical Research Laboratory, Washington, D. C., Government Printing Office, 1918, p. 156; in Air Service Medical, Washington, D. C., Government Printing Office, 1919, p. 275. Berens, C.; Hardy, L. H., and Pierce, H. F.: Studies in Ocular Fatigue, in Contributions to Ophthalmic Science, Dedicated to Dr. Edward Jackson, Menasha, Wis., George Banta Publishing Co., 1926, p. 102; Studies in Ocular Fatigue: II. Convergence Fatigue in Practice, Tr. Am. Ophth. Soc. **24**:262, 1926.

challenged by Lancaster and Williams, who suggested that the blurring he noted was retinal in origin.

Lancaster and Williams [3] studied fatigue of accommodation both by sustained near fixation and by repeated determinations of the near point of accommodation following intervals of the reading of fine print. Although both the punctum proximum and the punctum remotum were generally brought nearer in their experiments, they obtained some curves in which a slight falling off of power to accommodate occurred after about one-half hour of continuous fixation.

Howe [4] adapted Mosso's ergographic method of studying fatigue of striated muscle to the study of fatigue of the ocular muscles. The first ophthalmic ergograph was described in 1912. Howe obtained typical fatigue curves by tracing the progressive recession of the blur point of the test object on a kymograph.

Berens and Stark,[1a] following Howe's pioneering efforts, refined the ergographic technic and produced a number of modifications and improvements of Howe's original model. These authors [1b] reported on a study of two groups of records made in the testing of fatigue of accommodation with the ophthalmic ergograph. In the first group, 165 qualified and 14 disqualified aviators were tested under low oxygen tension. More rapid recession of the near point of accommodation was found than when the subjects were under normal oxygen tension. A second group of 195 records of fatigue of accommodation in office patients, most of whom were asthenopic, showed variation in type of records. Fatigue of accommodation was not easily produced even in this group of patients. A high positive correlation was noted between the objective and the subjective evidence of fatigue of accommodation. Duane's tables for the near point of accommodation for various age groups were found to be an unreliable criterion of ability to accommodate without rapid fatigue.

The results of these experimental studies indicated that the ophthalmic ergograph could be used with success as a clinical instrument, both for diagnosis of easy fatigability of accommodation and for neuromuscular training.

With the exception of the one series of observations on subjects under conditions producing anoxemia, however, no evidence has yet been obtained relating to significant factors which cause fatigue. The experiments reported here are a continuation of Berens' earlier work. They were designed to evaluate the significance of a number of factors generally regarded as important in relation to ocular fatigue under carefully controlled experimental conditions. The factors selected for experimental study were (*a*) intensity of illumination, (*b*) types of test objects, (*c*) age and (*d*) visual task.

PLAN OF RESEARCH

A series of experiments was designed to study the effect of a visual task involving use of the ophthalmic ergograph on clinic patients with complaints of ocular fatigue or other symptoms of asthenopia.

A number of experimental factors were varied systematically in accordance with the plan shown in table 1. The different experimental conditions were controlled by the device of using the same patients for each of the 12 experimental tasks. This method makes possible direct comparisons on a constant population.

In these experiments, the ergograph task was extended to a limit of thirty minutes. This period was twice that employed in most previous experiments. The extension of time was considered most important because it was our belief that failure to obtain records of fatigue in many previous cases was due to inadequate work samples. The results reported here confirm this hypothesis.

Experimental Design.—Table 1 presents schematically the design of the research. Each subject was tested in 12 experimental situations. Experiment 1 consisted of an ergograph

task for the right eye only, the Berens astigmatic cross being used for near vision as a test object for accommodation under 5 foot candles of illumination. Before the ergograph task the subject was tested for muscle balance at 6 meters (far vision) and at 25 cm. (near vision) with the Maddox rod, and the near points of accommodation of the right eye, of the left eye and of both eyes were measured under 10 foot candles of illumination. After a brief pause for adaptation the ergograph task was administered for a period not exceeding thirty minutes. Then the final measurements of muscle balance and the near point of accommodation were made as before.

Experiments 2 and 3 were identical with experiment 1 except that the ergograph task was administered to the left eye in experiment 2 and to both eyes in experiment 3. Experiments 4, 5 and 6 followed the same plan except that in this series the test object was a line of letters on the Berens accommodation card. In experiments 7, 8 and 9 the astigmatic cross was used under 50 foot candles of illumination, and in experiments 10, 11 and 12 the letters were used under 50 foot candles of illumination.

Table 1.—*Diagrammatic Schema of Experimental Design, Showing Sequence of Experiments and of Tests at Each Experiment, and Experimental Conditions* *

	Illumination			
	5 Foot Candles		50 Foot Candles	
	Test Object		Test Object	
Eye	Cross	Letters	Cross	Letters
	Experiment 1	Experiment 4	Experiment 7	Experiment 10
Right	(*a*) (*b*) (*c*) (*d*) (*e*)	(*a*) (*b*) (*c*) (*d*) (*e*)	(*a*) (*b*) (*c*) (*d*) (*e*)	(*a*) (*b*) (*c*) (*d*) (*e*)
	Experiment 2	Experiment 5	Experiment 8	Experiment 11
Left	(*a*) (*b*) (*c*) (*d*) (*e*)	(*a*) (*b*) (*c*) (*d*) (*e*)	(*a*) (*b*) (*c*) (*d*) (*e*)	(*a*) (*b*) (*c*) (*d*) (*e*)
	Experiment 3	Experiment 6	Experiment 9	Experiment 12
Both	(*a*) (*b*) (*c*) (*d*) (*e*)	(*a*) (*b*) (*c*) (*d*) (*e*)	(*a*) (*b*) (*c*) (*d*) (*e*)	(*a*) (*b*) (*c*) (*d*) (*e*)

* In this table *a* indicates initial near point of accommodation (10 foot candles), right eye, left eye, both eyes; *b*, initial muscle balance; *c*, ergograph test (5 or 50 foot candles, 30 min.); *d*, final near point of accommodation (10 foot candles), right eye, left eye, both eyes; *e*, final muscle balance.

Selection of Subjects.—One hundred and fifty clinic patients were referred for testing. Of these, 57 who completed all tests constituted the population for the present report. These subjects ranged in age from 9 to 54 years and were distributed according to the following age groups:

Age, Yr.	Males	Females	Total No.
6-10	3	5	8
11-15	9	19	28
16-20	6	5	11
21-25	..	3	3
26-30	1	..	1
31-35	..	1	1
36-40	1	2	3
41-45	..	1	1
46-50	..	..	..
51-55	1	..	1
Total	21	36	57

The subjects were selected by the clinic ophthalmologist on the basis of symptoms of asthenopia and complaints of ocular fatigue. Patients with pathologic conditions of the eyes squint, etc., were not referred.

Refraction with cycloplegia was performed on all patients before the tests were begun and they wore the recommended correction during the experiments. Normal vision of 20/20 was required, with manifest refraction showing not more than 1 D. of manifest hyperopia and 0.5 D. of hyperopic astigmatism, or with refraction with cycloplegia giving not more than 0.25 D. of myopia and 0.5 D. of myopic astigmatism.

The selection of clinic patients provided a homogeneous group with respect to socio-economic status.

High motivation was secured by the referring ophthalmologist by informing the patients that they were to receive exercises for the eye muscles. Because of this explanation, despite boredom and the inconvenience of their returning many times, the subjects were interested in knowing whether their "performance" was improving. A possible objection to this device is that patients have a tendency to want to improve and may thus delay the reporting of complete blurring or fatigue in later test sessions.

Apparatus.—The apparatus used in these experiments was an ophthalmic ergograph designed by one of us (C. B.)[6] for research (fig. 1). It was mounted on an adjustable table, which allowed accurate adjustment of height for each patient, as well as adjustment in height of the test object. This ophthalmic ergograph is the seventh reported by Berens.[6] With this instrument, the speed of forward and backward movement of the test

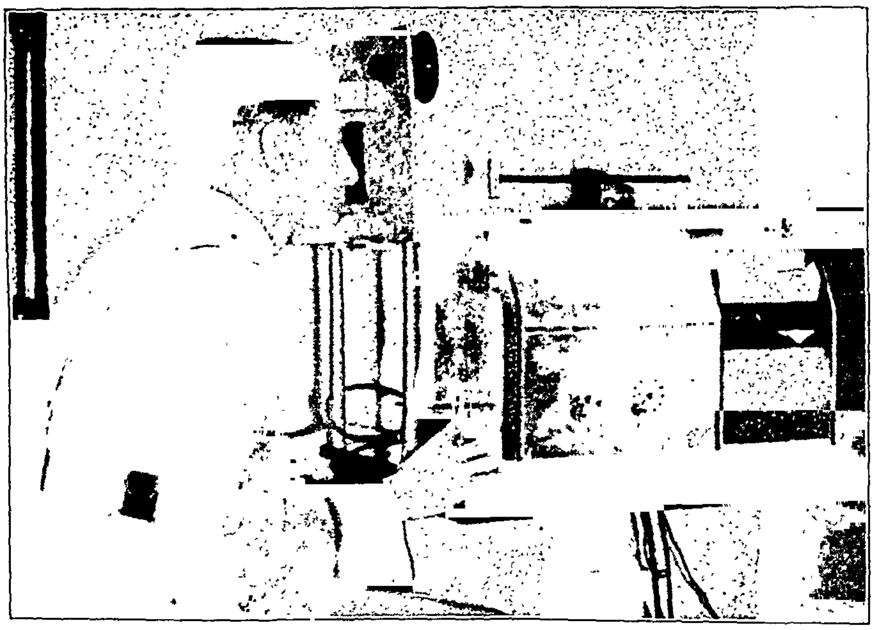


Fig. 1.—Accommodation ergograph.

object and the duration of the rest pause are controlled. The total range of movement of the test object carrier is 15 cm. A single motor drives the test object and the kymograph drum. The source of light is a single bulb mounted on the back of the screen above the chin rest, which projects light down on the test object carrier. This is a change from previous models, in which the light source was set on the test object carrier and was thus affected by the movements and vibration of the carrier. This ophthalmic ergograph is designed to reduce to a minimum all mechanical distraction and demands of mechanical control on the part of the subject. In addition to the change in method of illumination the following improvements were made: A new pen holder was devised for accuracy in recording; a shield of black cardboard was constructed in front of the recording device so that the patient was not distracted by the motion of the pen holder or by light reflecting in the vicinity of the ergograph; a Prince rule was set on the ergograph, and an opaque black cardboard screen was mounted before the ergograph, with an aperture so designed that it exposed to view only the test object. The light source was mounted on the inside of this screen; a chin rest and a head rest were substituted for the tongue depressor biting board previously employed. The tongue depressor was discarded because of the extreme discomfort to the subject during protracted, thirty minute test periods.

In the experiments reported here, the forward and backward speed of movement of the test object and the rest pause were constant throughout. The test object moved forward at

6. Berens, C.: An Accommodation Ergograph, Tr. Am. Acad. Ophth. **34**:472, 1929.

the rate of 2 cm. per second until stopped by the subject's pressing the control button (to indicate the point of blurring). Immediately after this, the test object returned to the point of origin at the same speed. The rest pause was two seconds.

Illumination.—Two experimental levels of illumination were used, 5 and 50 foot candles. These two levels were selected in order to obtain a noticeable difference within a practical range. A rheostat controlling the light source and a General Electric light meter mounted on the ergograph were used in calibration of the intensity of illumination at the following times: (1) at the start of each separate test session before measurement of the near point of accommodation for each eye separately and for both eyes; (2) during the test if any variation was noted in the mechanics of the setup for illumination; (3) if there was any change in the hum of the generator;[7] (4) if the patient remarked on any alteration in the lighting conditions, for example, fading or flickering, and (5) at the end of each test.

The illumination for measurement of the near points of accommodation and the muscle balance before and after each ergograph test was 10 foot candles.

During the period of rest between tests, the subject was given the choice of remaining in the darkened room or of having the room lighted artificially or by daylight.

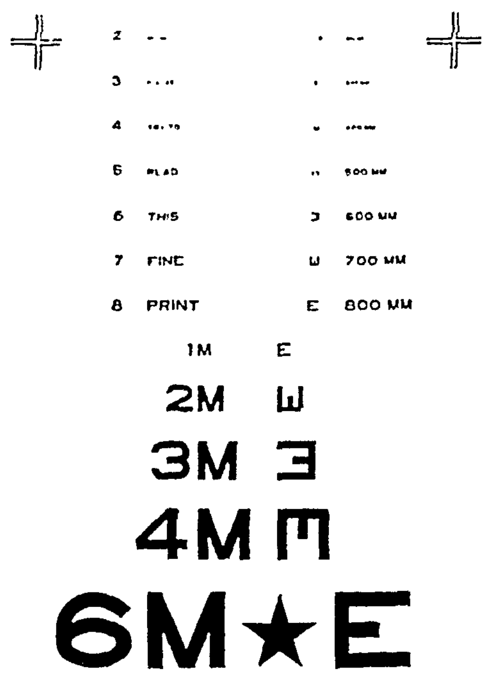


Fig. 2.—Accommodation test card; photographically reduced letters (Berens).

Test Objects.—The test objects used were the Berens astigmatic cross and photographically reduced letters on the Berens accommodation test card (fig. 2). These two types of test objects were selected because of their wide clinical use and because of their resemblance to visual material of importance in two significant life situations requiring fine near discrimination and accommodation. The cross resembles the crossed lines seen in gun and bomb sights. The letters are significant in reading.

Experimental Room.—The room was a small one with one window. During the tests, the window shades were drawn and a black cambric curtain was hung over the lower half. The transom was covered with a light-proof material. The walls were painted a dull pearl gray which had no important effect on the conditions of the test. Because of a building adjacent to the room the natural illumination was never great.

Experimental Procedure.—Each patient referred for study was examined for errors of refraction under cycloplegia before he reported for tests. At the first session the subject

7. The ergograph motor was on alternating current and the house current on direct current. The generator was used to convert the house current to alternating current. At certain times, when additional current was used elsewhere in the building, this caused a change in the exact level of illumination on the apparatus. Such changes were instantly recognized by a change in the sound of the generator.

was interviewed and the following preliminary information recorded: name; age at last birthday; sex; reading and visual habits; occupation and economic status, and visual complaint, based on the subject's own report. Data concerning visual acuity, correction to be worn during the experiment and results of refraction were provided from clinic records.

The experimenter explained the nature of the ergographic exercise to the subject and attempted to establish rapport with him by discussing his symptoms and giving him an opportunity to adjust to the test situation. Usually a preliminary demonstration of the ergograph was made.

At each experimental period the following procedure was observed:

1. The room was darkened, and muscle balance was determined at 6 meters, with a Maddox rod and prisms. Muscle balance was then taken at 25 cm.

2. A minute's rest was given, and then the subject was seated at the ergograph, wearing correcting lenses as prescribed. The correction was made with the use of trial frames if necessary.

3. The heights of the table, chair and test object were adjusted.

4. The near points of accommodation for the right eye, for the left eye and for both eyes under 10 foot candles of illumination were measured at the ergograph by the procedure already described. The test object for all these measurements was the astigmatic cross.

5. The subject was given a rest period of one minute, during which the illumination of 5 or 50 foot candles to be used during the ergograph experiment was calibrated.

6. The ergograph test was then administered for a period not exceeding thirty minutes. In a few cases the subject was permitted to continue slightly longer. The longest test recorded was thirty-nine minutes. The subject was instructed to remain silent during the test, to maintain fixation on the test object and to avoid movements of the head and body. Perfect compliance with these instructions was seldom obtained, and the experimenter recorded all deviations. Special instructions were given concerning the method of fixation. The subject was instructed to read the line of letters serially and to regard the cross, fixating its four arms in serial order. These instructions were designed to avoid retinal adaptation, which has often been confused with fatigue. At the end of the ergograph task the time was noted, and the reason for the subject's stopping was recorded as follows: L. R., limit reached; C. B., constant blur, or G. F., general fatigue or tiredness or inability to continue.

In cases in which the subject reported complete blurring of the test object his report was checked, to differentiate recession of the near point from purely visual fatigue, with a + 1.00 D. lens placed over his regular correction at the conclusion of the ergograph test. Most subjects reported improvement in ability to see the test object distinctly.

7. Immediately after this ergograph test the measurements of near point of accommodation under 10 foot candles of illumination were repeated.

8. After this, and after a rest period of one minute, the room was darkened slightly, and the measurements of muscle balance with the Maddox rod were repeated.

9. At the conclusion of experiment 1 the subject was allowed a rest period of at least five minutes, or until he had recovered completely from his blurring or fatigue and until the near point of accommodation had returned to normal. The same procedure was then repeated with the other eye (experiment 2) and then with both eyes (experiment 3). Whenever possible three tests with identical illumination and the same test object were given at a single sitting, unless there was excessive fatigue or the subject was unable to remain for sufficient time. The experimental arrangements were limited by the amount of time a subject had available. The complete experimental series required at least six hours of a subject's time. Each sitting averaged one and a half hours. The subject was requested to discuss his reaction after each test and often made a number of statements during the course of the test.

A standard setting of the distance, or base, position of the test object carrier was established for the experiments at the beginning of experiment 1. This was done by determining the near point of accommodation for each eye separately and then drawing the test object back 10 cm. from the average of these two points. The near points were determined in the following way: The test object was moved forward on the track manually by the experimenter, and the subject was instructed to report the moment the test object blurred. He was then asked to explain just what he perceived at this point. If the subject's response indicated that he understood the task, the same procedure was repeated four times and the median blur point calculated. Inasmuch as the range of movement of the test object carrier is 15 cm., this method provided for maximum forward movement of the test object to a point 5 cm. nearer the eye than the average of the near points of the two eyes. By this

procedure an objective check was provided on the subject's understanding of the ergograph task. The distance setting thus determined was used for all 12 experiments.

Instructions to Subjects.—Much attention was given to the instruction of the subjects in their task. The exact understanding of the blurring of the test object, and of how to recognize it and respond to it, is crucial to the successful interpretation of the results. Because of the differences in age, language background and intellectual level of the subjects tested, it was found impractical to use standard instructions for each subject. In general the instructions took the following form: "The cross seen before you will blur when it is close to your eyes, and you should indicate when it blurs by pressing the button. If there is a change in the condition of your eyes, that is, if you feel tired or if the cross blurs, you are to report this to me." This statement was repeated and elaborated as much as the experimenter thought necessary before the experiment was begun. The subject was instructed to look at the object carefully both as it came toward him and as it receded and to report any change in its appearance. The subject usually reported that it disappeared as it came up close. He was then asked to watch it several times and to report any change immediately before it disappeared. He usually reported: "it blurs"; "it gets fainter"; "I can't see it so well"; "there are two of them"; "the lines get fuzzy"; "the lines fade"; "it looks like it gets under water." If the subject did not use the word "blur," he was asked if at any time he noticed the test object blur. If he had, he was asked to explain what he meant by "blur." If necessary, the meaning of blur was explained in terms of change in the appearance of the test object. The subject was cautioned against waiting until the test object had disappeared and was instructed in the difference between blurring and doubling. The criterion of blurring was distinguished from that of disappearance.

The subject was instructed to hold his head steady in the chin and head rests and to fixate the test object continuously without shifting his gaze. Special instructions were given for fixating both the letter and the cross. In fixation of the cross he was told to fix on the quadrants of the cross in a clockwise fashion, counting them off 1, 2, 3, 4, silently. In fixation of the letters he was told to fix on each letter of the appropriate line serially.

The line of type read was the smallest line on the accommodation card which the subject could read easily at 10 to 14 inches (25 to 35 cm.). At first the entire card was exposed, and the subject was instructed to fixate the line read as previously described. Soon after the beginning of the experiments a mask was prepared which exposed only the line read.

The subject was instructed to press the button at the point of blurring on each forward trip of the carrier and to follow the test object on its return. He was instructed to give as detailed a subjective report as possible.

RESULTS

Recession of Near Point of Accommodation Following a Period of Interpolated Work on the Ophthalmic Ergograph.—In this paper the results of the 12 experiments for the entire group of 57 patients are presented with respect to changes in the near point of accommodation following the ergograph test. The specific data analyzed are the measurements of the recession of the near point of accommodation, separately for the right eye, for the left eye and for both eyes, under 10 foot candles of illumination after each ergograph test. This recession is expressed as the difference between the initial and the final mean near point. A statistical test of the significance of this difference is analyzed for evidence of fatigue of accommodation. This is the first study of ocular fatigue in the literature in which the work decrement is evaluated by a statistical test of significance. Earlier authors drew conclusions concerning the occurrence or nonoccurrence of fatigue on the basis of the analysis of so-called fatigue curves. In a later paper in this series it will be shown that evidence of fatigue, expressed as a decrement between the initial and the final near point of accommodation separated by an interpolated period of work on the ophthalmic ergograph, is obtained in many cases in which a typical "fatigue curve" does not occur.

In subsequent papers we shall present additional data in analysis of the effect of the various experimental factors: intensity of illumination; types of test objects; age, and visual task, with an analysis of the ergographic records and data relating to error of refraction, dominant eye and visual acuity, together with a more detailed analysis of individual cases.

Experiment 1 consisted of an ergograph test for the right eye only, with the left eye occluded; the experimental test object was the astigmatic cross, and the illumination, 5 foot candles. Table 2 presents the mean and the standard deviation of the initial and the final near points of accommodation, the mean differences and the critical ratios of the differences for each eye separately and for both eyes.

The test of significance used to evaluate the reliability of the differences between the initial and the final means is a critical ratio obtained by dividing each difference ($M_F - M_I$) by the standard error of that difference (S.D.$_{\text{Diff.}}$). A critical ratio of 1.64 indicates that the probability that a difference as great as that obtained could have occurred by chance is 95 chances in 100. The probability is 99 in 100 for a ratio of 2.20 and 99.9 in 100 for a ratio of 3. For a ratio of 5, it is 99.99997133 in 100. Most statisticians accept the 95 per cent value as reliable and the 99 per cent value as extremely reliable. A detailed treatment of this method may be found in the text by Peters and Van Voorhis.[8]

The initial and final means for the right eye are 10.49 and 13.37 cm. respectively. The difference is 2.88 cm., which is 6.13 times the standard error of the dif-

TABLE 2.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 1; right eye; cross; 5 foot candles) *

Eye	Initial N. P. A. Mean	Initial N. P. A. Standard Deviation	Final N. P. A. Mean	Final N. P. A. Standard Deviation	Difference ($M_F - M_I$)	Critical † Ratio (D/S.D. Diff.)
Right	10.49	2.49	13.37	4.53	2.88	6.13
Left	10.91	2.91	12.49	4.03	1.58	4.27
Both	9.46	2.31	11.04	3.25	1.58	4.39

* In this table, and in the accompanying tables, the values represent data obtained with the ergograph test on a total of 57 subjects who completed all the tests. The near points of accommodation are always expressed in centimeters.

N. P. A. indicates near point of accommodation; M_F, final mean; M_I, initial mean; D, difference; S.D., standard deviation of distribution and Diff., difference.

† The following formula was used in computing all critical ratios:

$$\text{C. R.} = \frac{\text{Difference } (M_F - M_I)}{\text{S.D.}_{(\text{Diff.})}}, \text{ in which S.D.}_{(\text{Diff.})} = \sqrt{\text{S.D.}^2_{M_I} + \text{S.D.}^2_{M_F} - 2r_{IF}\ \text{S.D.}_{M_I}\ \text{S.D.}_{M_F}}$$

(Peters and Van Voorhis,[8] chap. V and VI.)

ference. The initial and final means for the left eye are 10.91 and 12.49 cm. respectively. The difference is 1.58 cm., which is 4.27 times the standard error of the difference. The initial and final means for both eyes are 9.46 and 11.04 cm. respectively. The difference is 1.58 cm., which is 4.39 times the standard error of the difference. The magnitude of the corresponding critical ratios indicates that these differences could not have occurred by chance. The difference is greatest for the right eye, as is the critical ratio for that difference.

Tables 3 through 13 are identical in design with table 2. They show the results of experiments 2 through 12 respectively. All of the differences reported are statistically significant. The interpretation of these tables follows exactly the same pattern as that of table 2. In general, the difference in means is greatest and the critical ratio is highest for the working eye (or working eyes, when both eyes were tested together).

In experiment 2 the difference in the means is greatest for the left eye, as is the corresponding critical ratio. It is noted that similar differences and critical ratios were obtained for the right eye and for both eyes (table 3).

8. Peters, C. C., and Van Voorhis, W. R.: Statistical Procedures and Their Mathematical Bases, New York, McGraw-Hill Book Company, Inc., 1940, chap. 5 and 6.

In experiment 3, although the difference between the initial and the final mean is greatest for the left eye, the range of the three differences in means is only 0.25 cm. (table 4). The critical ratio is greatest for the difference in the means for both eyes.

TABLE 3.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 2; left eye; cross; 5 foot candles)

	Initial N. P. A.		Final N. P. A.			
Eye	Mean	Standard Deviation	Mean	Standard Deviation	Difference (MF — MI)	Critical Ratio (D/S.D. Diff.)
Right	10.68	4.24	12.47	4.26	1.79	2.80
Left	10.81	2.58	13.61	4.78	2.80	5.72
Both	9.98	2.66	11.25	3.82	1.27	2.89

TABLE 4.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 3; both eyes; cross; 5 foot candles)

	Initial N. P. A.		Final N. P. A.			
Eye	Mean	Standard Deviation	Mean	Standard Deviation	Difference (MF — MI)	Critical Ratio (D/S.D. Diff.)
Right	10.75	3.94	12.60	4.15	1.85	3.25
Left	10.60	2.53	12.70	4.48	2.10	2.84
Both	10.21	2.93	12.25	5.31	2.04	3.65

TABLE 5.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 4; right eye; letter; 5 foot candles)

	Initial N. P. A.		Final N. P. A.			
Eye	Mean	Standard Deviation	Mean	Standard Deviation	Difference (MF — MI)	Critical Ratio (D/S.D. Diff.)
Right	11.02	2.95	13.56	5.03	2.54	5.19
Left	10.89	2.82	12.75	4.51	1.86	4.53
Both	10.02	2.94	11.97	4.42	1.95	5.00

TABLE 6.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 5; left eye; letter; 5 foot candles)

	Initial N. P. A.		Final N. P. A.			
Eye	Mean	Standard Deviation	Mean	Standard Deviation	Difference (MF — MI)	Critical Ratio (D/S.D. Diff.)
Right	11.23	3.17	13.02	4.30	1.79	4.84
Left	11.25	3.29	13.79	4.85	2.54	6.05
Both	10.51	3.18	11.89	4.47	1.38	3.94

In experiment 4 the difference between the initial and the final mean is greatest for the right eye, as is the critical ratio for that eye. The differences in the means and the critical ratios are similar for the left eye and for both eyes (table 5).

In experiment 5 the difference between the initial and the final mean is greatest for the left eye, as is the critical ratio for that eye (table 6).

In experiment 6 the difference between the initial and the final mean is greatest for both eyes, as is the corresponding critical ratio. The differences in the means and the critical ratios for the right and the left eye are approximately equal (table 7).

TABLE 7.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 6; both eyes; letter; 5 foot candles)

Eye	Initial N. P. A. Mean	Initial N. P. A. Standard Deviation	Final N. P. A. Mean	Final N. P. A. Standard Deviation	Difference (MF — MI)	Critical Ratio (D/S.D. Diff.)
Right	10.84	2.54	12.18	4.41	1.34	3.83
Left	10.88	2.83	12.25	4.72	1.37	3.34
Both	10.46	3.02	12.16	4.74	1.70	4.47

TABLE 8.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 7; right eye; cross; 50 foot candles)

Eye	Initial N. P. A. Mean	Initial N. P. A. Standard Deviation	Final N. P. A. Mean	Final N. P. A. Standard Deviation	Difference (MF — MI)	Critical Ratio (D/S.D. Diff.)
Right	10.96	2.81	12.77	4.61	1.81	4.90
Left	11.00	3.06	12.35	4.48	1.35	3.30
Both	10.05	2.78	11.89	4.35	1.84	4.00

TABLE 9.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 8; left eye; cross; 50 foot candles)

Eye	Initial N. P. A. Mean	Initial N. P. A. Standard Deviation	Final N. P. A. Mean	Final N. P. A. Standard Deviation	Difference (MF — MI)	Critical Ratio (D/S.D. Diff.)
Right	10.67	3.14	12.44	5.19	1.77	3.85
Left	10.89	3.11	13.14	5.04	2.25	5.00
Both	10.12	2.78	11.75	4.10	1.63	3.70

TABLE 10.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 9; both eyes; cross; 50 foot candles)

Eye	Initial N. P. A. Mean	Initial N. P. A. Standard Deviation	Final N. P. A. Mean	Final N. P. A. Standard Deviation	Difference (MF — MI)	Critical Ratio (D/S.D. Diff.)
Right	10.67	3.13	12.65	4.88	1.98	4.95
Left	10.67	3.29	12.56	4.64	1.89	4.72
Both	10.00	3.09	12.44	5.42	2.44	5.95

In experiment 7, although the difference between the initial and the final mean is greatest for both eyes, it is only 0.03 cm. greater than that for the right eye. The critical ratio is greatest for the right eye. The difference in means is least for the left eye, as is the critical ratio for that eye (table 8).

In experiment 8 the difference between the initial and the final mean is greatest for the left eye, as is the critical ratio for that eye (table 9). The differences in the means for the right eye and for both eyes are similar.

In experiment 9 the difference between the initial and the final mean is greatest for both eyes, as is the corresponding critical ratio. The differences in the means and the critical ratios for the right eye and for the left eye are smaller and are approximately equal (table 10).

In experiment 10 the difference in the means is greatest for the right eye, as is the critical ratio for that eye (table 11).

In experiment 11 the difference between the initial and the final mean is greatest for the left eye, but the critical ratio is greatest for the right eye (table 12). The

TABLE 11.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 10; right eye; letter; 50 foot candles)

	Initial N. P. A.		Final N. P. A.			
Eye	Mean	Standard Deviation	Mean	Standard Deviation	Difference (MF — MI)	Critical Ratio (D/S.D. Diff.)
Right	10.54	2.71	13.09	4.83	2.55	6.22
Left	10.40	2.82	12.30	4.66	1.90	4.87
Both	9.80	2.08	11.61	4.26	1.81	4.52

TABLE 12.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 11; left eye; letter; 50 foot candles)

	Initial N. P. A.		Final N. P. A.			
Eye	Mean	Standard Deviation	Mean	Standard Deviation	Difference (MF — MI)	Critical Ratio (D/S.D. Diff.)
Right	10.56	2.28	12.28	4.14	1.72	5.40
Left	10.53	2.87	12.96	5.17	2.43	5.40
Both	9.91	2.64	11.75	4.13	1.84	5.10

TABLE 13.—*Comparison of Mean Initial and Final Near Points of Accommodation for the Right Eye, for the Left Eye and for Both Eyes* (experiment 12; both eyes; letter; 50 foot candles)

	Initial N. P. A.		Final N. P. A.			
Eye	Mean	Standard Deviation	Mean	Standard Deviation	Difference (MF — MI)	Critical Ratio (D/S.D. Diff.)
Right	10.54	3.25	12.21	4.75	1.67	3.71
Left	10.58	3.05	12.35	5.18	1.77	3.94
Both	9.82	2.83	12.42	6.26	2.60	4.26

critical ratio of 57.40 is accounted for by a correlation of 0.94 between the initial and the final near point of accommodation.

In experiment 12 the difference between the initial and the final mean is greatest for both eyes, as is the corresponding critical ratio. The differences in the means and the critical ratios for the right and the left eye are approximately equal (table 13).

COMMENT AND SUMMARY OF RESULTS

1. Evidence of Occurrence of Fatigue of Accommodation.—The results of a partial analysis of 12 experiments on the fatigue of accommodation with use of the Howe-Berens ophthalmic ergograph which have been reported are concerned with evidence of the occurrence of such fatigue; the data analyzed are differences

between mean near points of accommodation computed from measurements of near points taken for the 57 subjects, at 10 foot candles of illumination, immediately before and after each ergograph experiment.

The initial and final mean near points of accommodation for the right eye, for the left eye and for both eyes were compared for each experiment, and critical ratios were obtained by dividing each difference in the means by the standard error of the difference. Of the 36 critical ratios so computed, 33 were greater than 3. The three remaining ratios were 2.80, 2.84 and 2.89 respectively. In terms of probability, a critical ratio of 3 means that the chances are 99.9 in 100 that the difference obtained could not have occurred by chance. A critical ratio of 2.80 indicates that the chances are greater than 99 in 100 that the observed difference did not occur by chance.

We conclude, then, that the differences between all initial and final mean near points are statistically significant. Because of the experimental design, we conclude, further, that the differences represent a recession of the near points as a result of the interpolated periods of exercise on the ophthalmic ergograph. This is regarded as evidence of fatigue of accommodation.

2. *Differential Effects on the "Working Eye" and the Occluded Eye.*—Experiments 1, 4, 7 and 10 were performed on the right eye, with the left eye occluded. In experiments 1, 4 and 10 the difference between the initial and the final mean point of accommodation was greater for the right eye than for the left eye or for both eyes, and the corresponding critical ratios were similarly greater. The difference in means was greatest for both eyes in experiment 7, but this difference was only slightly larger than that for the right eye.

Experiments 2, 5, 8 and 11 were performed on the left eye, with the right eye occluded. In all 4 of these experiments the differences in the means for the left eye exceeded greatly those for the right eye and for both eyes. The corresponding critical ratios for these differences were distributed in the same relations in experiments 2, 5 and 8.

Experiments 3, 6, 9 and 12 were performed on both eyes. The differences in means in experiments 6, 9 and 12 were greatest for both eyes. The difference in the means for the left eye was slightly greater than that for both eyes in experiment 3. All critical ratios for both eyes were highest in this series.

These results confirm the expectation that both eyes will manifest fatigue, even when only one works while the other is occluded. The effect is differential, however, and the "working eye" loses accommodative power temporarily (fatigues) to a greater extent than the other, which merely accommodates reciprocally because of neuromuscular interaction.

Miss Alice Gilman administered the experiments reported.

35 East Seventieth Street.

OPHTHALMIC REQUIREMENTS OF THE MILITARY SERVICES

CHANGES FROM FEB. 1, 1943 TO JAN. 1, 1944

CHARLES A. BAHN, M.D.

NEW ORLEANS

At the request of the American Committee on Optics and Visual Physiology, the following changes are presented. For details the reader is referred to the original article.[1]

SELECTIVE SERVICE

Sections 1, 2 and 3 are unchanged.

ARMY

In section 1, requirements indicated under the headings "Vision," "Refraction," "Color Vision" and "Muscles" are unchanged except for the following regulation, which applies to enlisted personnel, general service:

Binocular vision (both eyes open) of not less than 20/40, without glasses, provided vision in the more defective eye is not less than 20/70 without glasses, correctable or uncorrected, and provided the defective vision is not due to organic disease.

Section 2 is unchanged.

Section 3 is unchanged except for the authority for the new regulation in section 1.

Letter from the War Department, Army Service Forces, Office of the Surgeon General, Washington, D. C., Nov. 15, 1943.

NAVY, MARINE CORPS AND MERCHANT MARINE

Section 1.—The functional requirements for enlisted and commissioned personnel, male and female, in the Navy, Marine Corps and Merchant Marine are as follows:

	Vision				
	Without Glasses		With Glasses		Color Vision (Tests Conducted with Pseudoisochromatic Plates for Testing Color Perception; American Optical Company or Stilling Test)
	One Eye	Other Eye	One Eye	Other Eye	
1. Enlisted personnel...................... Navy (regular), Marine Corps (regular)	15/20	15/20	20/20	20/20	Must read one plate of each of the following groups of American Optical Company's plates: (1) plates 1, 2, 3, 4; (2) plates 7, 8, 9, 10, 13, 14, and (3) plates 17, 18, 21, [illegible] (these groups are represented in Stilling's twentieth edition † by plates 3, 4 and 8)
Navy (reserve), Marine Corps (reserve)	6/20	10/20	No lens correction necessary		Same requirements as for regular enlisted personnel; defective color perception may be waived for induction or enlistment in class V6 (Seabees)
	No organic disease				
	[Binocular]				
Waves (Navy); Marine Corps; Women's Reserve, class VI (a)	6/20	12/20	20/20	20/20	Same requirements as for regular enlisted personnel
	No organic disease; defective vision not due to organic disease and correctable to 20/20 may be waived locally				
Inductees in Navy and Marine Corps	6/20	10/20	No lens correction necessary		Same requirements as for regular enlisted personnel
	Or 10/20 binocular with minimum of 6/20 in either eye; no organic diseases				
Inductees for special assignment	2/20	2/20	10/20	10/20	Color blindness acceptable
	Will accept slight functional defects				
2. Commissioned officers; line officers of Navy, regular and reserve (D = V [G] and DE = V [G] only) and line and staff officers of Marine Corps, regular and reserve	18/20	18/20	20/20	20/20	Must be able to read all pseudoisochromatic plates of American Optical Company or Stilling test
3. Commissioned officers (staff), civil engineers, Supply Corps, Medical Corps, Nursing Corps, Dental Corps and Chaplain Corps; line officers of Naval Reserve for special service; Seabees; commissioned Waves and commissioned officers of Marine Corps Women's Reserve	12/20	12/20	20/20	20/20	Must complete one of the two tests
4. Aviation officers, Navy and Marine Corps (involving actual control of aircraft)	20/20	20/20	.....	.....	Must complete one of the two tests
5. Naval Academy	20/20	20/20	.....	.....	Must complete one of the two tests
	No myopia or myopic astigmatism with homatropine cycloplegia				
6. Enlisted Reserve (potential officers):					
Class V1-G, class V1-S, class V7-G, class V7-S	Enlistments in these classes have been discontinued				
Class V-5..............................	20/20	20/20	.....	.....	
Class V-12, class V-12 (S), class SV-7 (S), class SV-12 (S) Midshipmen of Merchant Marine	18/20	18/20	20/20	20/20	Must complete one of the two tests
7. Merchant Marine, class M-1, M-2	Enlistments in these classes have been discontinued				

* American Optical Company: Pseudo-Isochromatic Plates for Testing Color Perception, Southbridge, Mass., American Optical Company, 1940.

† Stilling, J.: Stillings pseudo-isochromatische Tafeln zur Prüfung des Farbensinnes, ed. 20, Leipzig, G. Thieme, 1939.

From the Department of Ophthalmology, Medical Center, Louisiana State University School of Medicine.

1. Bahn, C. A.: (*a*) Ophthalmic Requirements of the Military Services, Arch. Ophth. **27**:1202-1213 (June) 1942; (*b*) **29**:831 (May) 1943.

The last footnote on page 6 of the Feb. 1, 943 revision of "Ophthalmic Requirements of he Military Services" (page 836 [1b]) has been nodified as follows:

The classes open for enlistment in the United States Naval Reserve are as follows: V5, aviation cadets for flight training; SV-7(S), pretheological students; V6 and V6SV, enlisted reserve; V9, enlisted Waves; V10, officer candidate Waves; V12, SV-12, V-12(S) and SV-12(S), men enlisted for Navy College Training rogram.

The classes open for enlistment in the United States arine Corps Reserve are as follows: III (b), enlisted id reenlisted men; SS III (b), transfers from induc-on; IV, limited duty, guard duty in the United States nly; V (b), specialist reservists; VI (a), women officer andidates, and VI (b), women enlisted.

The conditions of the eye listed on pages 4 and , section 2, paragraphs A and B of the Feb. 1, 943 revision of "Ophthalmic Requirements of ie Military Services" (page 834 [1b]) apply to iductees in the United States Navy and the Jnited States Marine Corps.

There are no changes in section 2, page 7, of he Feb. 1, 1943 revision of "Ophthalmic Re-uirements of the Military Services" (page 837 [1b]) relative to the disqualifying conditions l diseases for enlisted and commissioned sonnel.

References 4, 5, 6, 7 and 8 on page 7, section of the Feb. 1, 1943 revision of "Ophthalmic quirements of the Military Services" have n canceled (page 837 [1b]), and the following erences should be added:

1. Recruiting Circular Letter 7-43 Procurement Directive 6-43, Jan. 28, 1943.
2. Recruiting Circular Letter 24-43, June 1, 1943, United States Navy Department: enclosure C.
3. Recruiting Circular Letter 25-43, June 16, 1943, United States Navy Department: enclosure A.
4. Conference call to all officers of Naval Officer Procurement, June 5, 1943, United States Navy Department.
5. The Commandant, United States Marine Corps, letter of July 28, 1943 to the Officer in Charge of Procurement Divisions.
6. Bureau of Naval Personnel Letter, United States Navy Department, to the Navy Recruiting Service of May 26, 1943, Pers-620-RS, 5-26-43.
7. Bureau of Naval Personnel Letter, United States Navy Department, of Sept. 4, 1943, Pers-626-ACK.
8. Headquarters, United States Marine Corps Letter of July 24, 1943 to Officer in Charge of Procurement Division, MC-91894 1865-20 DHD-509-RSW.
9. Recruiting Circular Letter 28-43, July 13, 1943, United States Navy Department.
10. Headquarters, United States Marine Corps Letter, June 12, 1943, reference 1535-85 DHD-274-RSW (no serial number).
11. Headquarters, United States Marine Corps Letter of Instruction, Feb. 11, 1943, 1535-85 AQ-311-rwg.

COAST GUARD

Sections 1, 2 and 3 are unchanged.

AIR CORPS: ARMY AND NAVY

The requirements are unchanged except for those pertaining to the Army Air Corps.

The minimum requirements for visual acuity for aviation cadet training (air crew) and for officer training in grade (air crew) are 20/30, correctable to 20/20 in each eye. The efficiency of the extrinsic ocular muscles may permit esophoria of 12 D., exophoria of 7 D, and power of divergence of 2 to 15 prism diopters, equal to or greater than the number of diopters of esophoria. This test is accomplished at 20 feet (6 meters). Corrected depth perception is 35 mm.

The foregoing regulation has the following authority:

Relaxation in Physical Standard Requirements of Applicants for Air Crew Training, United States War Department, Circular 176.

UNITED STATES PUBLIC HEALTH SERVICE

The requirements are unchanged.

The committee acknowledges the cooperation and assistance of Surgeon General Norman T. Kirk and Lieutenant Colonel G. E. Gorman, of the Army, and Surgeon General Ross T. McIntire, of the Navy.

1703 Pere Marquette Building.

Clinical Notes

PENICILLIN IN TREATMENT OF GONORRHEAL CONJUNCTIVITIS

Report of a Case

WALTER P. GRIFFEY, M.D., NEW YORK

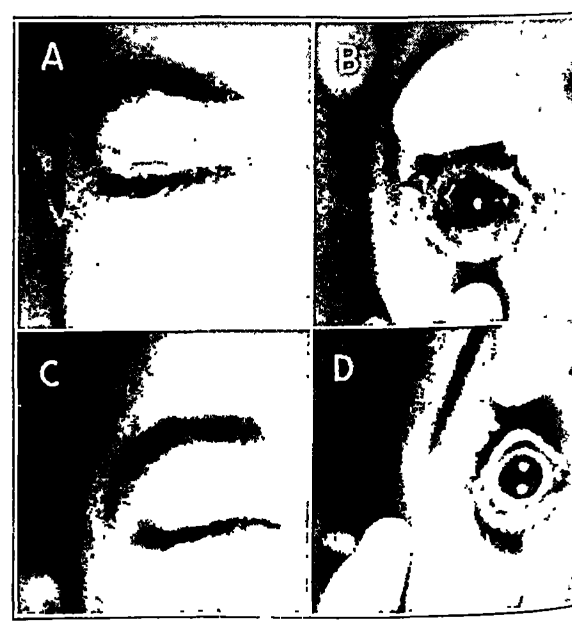
V. R., a man aged 24, was admitted to the United States Marine Hospital, Staten Island, N. Y., on July 3, 1943. He stated that a urethral discharge was observed on May 18, three days after sexual exposure. About four days subsequent to the appearance of the urethral discharge the patient noticed that the right eye was inflamed. On May 24 he was admitted to the United States Marine Hospital at Brighton, Mass., where the diagnoses of gonorrheal urethritis and gonorrheal conjunctivitis (of the right eye) were recorded. Sulfathiazole therapy was instituted, and sulfathiazole ointment, boric acid and cold compresses were applied locally. Bacterial vaccine made from the typhoid bacillus U. S. P. was given intravenously. The oral use of sulfathiazole was continued until July 2, at which time the urethral discharge had subsided considerably but the ocular infection, with a copious purulent discharge, persisted.

The appearance of the right eye at the time of admission to this hospital is shown in *A* and *B* of the accompanying figure. Spreads of the exudate from the conjunctival sac disclosed gram-negative intracellular diplococci, which were identified as gonococci by culture studies. The gonococcus was also identified by culture of sediment from the urine.

Therapy consisted of intramuscular injections of 25,000 units of penicillin sodium every three hours for a total of ten injections. The drug was dissolved in distilled water; the gluteal muscles were the sites of injection, and a 1½ inch (3.8 cm.) 22 gage needle was employed.

As a means of observation of the bactericidal effect of the therapy, hourly examinations of spreads and cultures of the conjunctival secretions were made. Both were recorded as positive for Neisseria gonorrhoeae for five hours, after which the results of examination were persistently negative. Specimens of urine were obtained at the beginning of therapy, three hours later and, again, five and one-half hours after institution of treatment. Cultures of sediment of the specimen taken at the beginning of treatment and of that obtained three hours after treatment had begun were recorded as positive for the organism. The culture of sediment from the specimen collected five and one-half hours after the beginning of treatment was recorded as negative. Subsequent studies of prostatic secretions gave uniformly negative results.

The clinical response was prompt. Approximately ten hours after the beginning of penicillin therapy the exudate of the eye had greatly diminished, and after the inflammation subsided the eye returned to normal



A and *B*, appearance of the eye before, and *C* and *D* appearance after, treatment with penicillin.

No other medication was used except for the instillation of a 1 per cent solution of atropine sulfate. At the time of discharge from the hospital vision in the left eye was 20/20 and the eye was normal. Vision in the right eye was 20/20 with correction with a +0.[illegible] D. sphere. *C* and *D* of the figure show the appearance of the eye after treatment.

The bacteriologic studies reported here were made by Dr. J. Durward Thayer, Venereal Disease Research Laboratory, United States Marine Hospital, Staten Island, N. Y.

From the United States Public Health Service.

This study was undertaken at the request of the Committee on Chemotherapeutic and Other Agents, Division of Medical Sciences, National Research Council, acting for the Committee on Medical Research of the Office of Scientific Research and Development. The penicillin was furnished through a contract between the Office of Scientific Research and Development and the Massachusetts Memorial Hospitals.

COMPARISON OF THE ISHIHARA AND THE AMERICAN OPTICAL COMPANY SERIES OF PSEUDOISOCHROMATIC PLATES

Captain Robert H. Harris, Medical Corps, Army of the United States

It has been noted that aviation cadet applicants sometimes pass the American Optical Company series of pseudoisochromatic plates but fail the Ishihara series. Fourteen hundred and seventy-one applicants for air crew training were examined by use of the 32 plate Ishihara series, followed by the 46 plate American Optical Company series. The applicant failed if he missed 25 per cent or more of the plates in each book.

It was found that 6.6 per cent, or 100, failed the Ishihara series, and 5.7 per cent, or 83, the American Optical Company series. Only 5 of the 83 who failed the American Optical Company series could not trace the gray-blue line in plate 35 of that series, and only 13 of the 100 candidates who failed the Ishihara series did not trace the two gray-blue lines in plates 30 and 31. Fifty-seven of the 83 candidates who failed the American Optical Company series missed a number in one or both of the gray-blue–numbered plates 33 and 34 of that series. Forty of the 100 candidates who failed the Ishihara series missed a number in one or more of the gray-blue–numbered plates, 18, 19, 20 and 21. These are the plates more easily read by persons who show some degree of color blindness, but they are usually read as blanks by applicants who have normal color vision. The ratio of candidates confusing the darker red with the brighter red in plates 22, 23, 24 and 25 in the Ishihara series was about 2 to 1.

One of the 17 men who passed the American Optical Company series received a perfect score but failed on 9 of the Ishihara plates, and another of these 17 men failed to read numbers in plates 32 and 34 of the American Optical Company series, although he read all the rest of the plates correctly, but failed on 18 of the Ishihara plates. Confusion of the number 3 with 8 or 5, of 7 with 2, of 4 with 1, of 9 with 3, of 7 with 9, of 6 with 8 or of 3 with 8 was noted many times with persons who had normal color perception.

Line plate 27 of the Ishihara series was passed by only 4 and line plate 29 by only 2 of the 100 candidates who failed in this series. The use of these plates alone therefore would have resulted in detection of a larger proportion of color-blind applicants than employment of all the tests in the American Optical Company series. Line plate 35 in the American Optical Company series was passed by 50 and line plate 36 by 15 of the 100 candidates who failed in the Ishihara series.

Acknowledgment of familiarity with the American Optical Company plates was obtained from some examinees. This series seemed more available for study than the Ishihara series. Some applicants who had previously failed in the color vision test returned after they had gained familiarity with the plates and requested another examination. Repeated color vision tests make possible better scores even when the order of presentation of the plates is varied. The examinee may fail when he first sees the plates, but on reexamination his score is improved. The ideal method is presentation of an unfamiliar series to the applicant, but this is not always possible. Attempts to check the history of previous familiarity with the American Optical Company series was met with evasion by many candidates who failed the Ishihara series but passed the American Optical Company series.

It has been recommended that in the examination of applicants for flying training the milder grades of color blindness should be detected and the candidates eliminated. Familiarity with tests does not mean improvement of deficient color vision. The examinee should be reexamined once. Nervous tension decreases the applicant's efficiency in reading the test. If he realized he was failing, his efficiency decreased. An applicant who was disqualified because of deficient color vision, if not previously aware of the defect, was usually more perturbed than by any other disqualification during the examination.

Because the line plates are placed at the end of the Ishihara book and are more time consuming, a candidate who fails more than 25 per cent of the plates before reaching this point is examined more rapidly. The line plates of the Ishihara series are much more efficient than the line plates of the American Optical Company series. The reason for the difference in efficiency of the duplicate line plates of the Ishihara and the

American Optical Company series is probably the difference in the artist's conception of color intensity. From the results in these tests the human eye seems to be the only factor concerned in testing and standardizing the color intensity of the plates. The perfect choice of varying color intensities in the Ishihara book leaves little to be improved on.

A few suggestions for improvement of the Ishihara plates from the standpoint of mass efficiency may be made:

Plate 1 of the book should consist of large ½ to 1 inch (1.27 to 2.54 cm.) circles of pure red, green and orange and varying shades with a white background. This plate could be used to distinguish pure red and pure green.

Plates 18 and 19, the two plates with blue-gray single numbers, as well as plate 39, with gray-blue lines, should be eliminated as superfluous.

Plate 32 should be placed before plate 26 as an instruction plate.

Test books for color vision should be stored in places where they not only are not exposed to light, but are not available for study by prospective color-deficient candidates.

CONCLUSIONS

The Ishihara series of plates seemingly meets the demands of mass efficiency better than the American Optical Company series because less time is consumed in the examination, elimination of candidates with subnormal color perception is more thorough and the book is less easily available to color-deficient candidates who wish to become familiar with it for the purpose of passing the examination.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

PENICILLIN AND GRAMICIDIN AS OCULAR CHEMOTHERAPEUTIC AGENTS

WAYNE W. WONG, M.D

CHICAGO

The discovery of two new chemotherapeutic agents from microbial sources has recently been reported. Their clinical application in treatment of local and systemic infections has demonstrated their effective antibacterial action, which appears to be more potent than that of any known chemotherapeutic agent. The few published reports regarding their utilization in ophthalmology have been somewhat dramatic; however, it appears from the small number of cases reported that the therapeutic potentialities of these agents have not been fully recognized by ophthalmologists.

The observation made by Pasteur and Jouber [1] in 1877 that the infective power of the anthrax bacillus was decreased when its growth was contaminated by certain saprophytic bacteria is apparently the first report of the phenomenon of antagonism between different microbial species. The therapeutic value of microbial antagonism was soon recognized, for by 1900 several reports appeared in regard to the use of an extract from cultures of Pseudomonas pyocyanea in the treatment of a variety of local infections. However, the great toxicity of this extract rendered it of little practical value.

In 1929 Fleming [2] observed that a strain of Penicillium notatum, a fungus, growing as a contaminant on nutrient agar plates, inhibited the growth of pyogenic cocci. This antagonistic activity was traced to a soluble principle, penicillin, present in the culture filtrates of the organisms. Fleming noted that the addition of penicillin to nutrient broth or agar inhibited the growth of most gram-positive organisms, whereas the gram-negative organisms remained unaffected. He further observed that the injection of broth containing penicillin was no more toxic to mice than plain broth, and he therefore suggested that this substance might be a useful antiseptic for application to infected wounds. Nothing further was reported concerning this substance until Chain and his associates,[3] in 1940, published their studies on the nature, properties and clinical advantages of penicillin.

The production of penicillin in therapeutic quantities is a long and tedious process. In 1941 Abraham and his co-workers [4] published their method for the mass production of this substance. Briefly described, their method is as follows: Batches of fifty vessels, each vessel containing 1,000 cc. of medium, are set up daily. These are autoclaved for an hour and inoculated on the following day with a spore suspension derived from subcultures of a strain of Penicillium used by Fleming. The greatest care is taken to avoid contamination, as even very small numbers of certain bacteria can reduce the yield of penicillin to the vanishing point. In about ten days the growth covers the surface of the medium, at which time the liquid containing the penicillin is drawn off. From this crude liquid, therapeutic penicillin is extracted with amyl acetate and purified by multiple chemical processes. About 100 liters of medium is required to produce 1 Gm. of therapeutic penicillin.

Penicillin has not yet been obtained in its crystalline form,[5] but spectrographic studies made by Holiday [6] revealed that the limit of purity of this substance thus far obtained has not been reached. It is readily soluble in organic solvents, is easily destroyed by acid reactions and is

From the Department of Ophthalmology, Cook County Hospital.

1. Pasteur, L., and Jouber, J.: Compt. rend. Acad. d. sc. **85**:101, 1877; cited by Dubos, R. J.: Bacteriostatic and Bactericidal Agents Obtained from Saprophytic Microorganisms, J. Pediat. **19**:588-595, 1941.

2. Fleming, A.: On the Antibacterial Action of Cultures of Penicillium with Special Reference to Their Use in the Isolation of B. influenzae, Brit. J. Exper. Path. **10**:226-236, 1929.

3. Chain, E.; Florey, H. W.; Gardner, A. D.; Heathley, N. G.; Jennings, M. A.; Orr Ewing, J., and Sanders, A. G.: Penicillin as a Chemotherapeutic Agent, Lancet **2**:226-228, 1940.

4. Abraham, E. P.; Chain, E.; Fletcher, C. M.; Gardner, A D.; Heathley, N. G.; Jennings, M. A., and Florey, H. W.: Further Observations on Penicillin, Lancet **2**:177-188, 1941.

5. Abraham, E. P., and Chain, E.: Purification and Some Physical and Chemical Properties of Penicillin, Brit. J. Exper. Path. **23**:103-115, 1942.

6. Holiday, G. L.: Spectrographic Examination of Penicillin Preparation, Brit. J. Exper. Path. **23**:115-119, 1942.

fairly stable in the form of the sodium or the barium salt.

Purified penicillin has an extremely powerful bacteriostatic action.[7] It is capable of inhibiting the growth of Staphylococcus aureus at a dilution of between 1:24,000,000 and 1:30,000,000. The standard of activity is the so-called Oxford unit, which may be defined as the amount of penicillin per milligram just capable of inhibiting a growth of Staph. aureus at a dilution of 1:50,000. Nothing is known of its mode of action, but it appears to prevent cellular division and gives rise to giant forms. The morphologic changes occurred even when the concentration of penicillin had no bacteriostatic effects.[8] No harmful effects on the blood elements have been reported.[9] Hobby and her associates [10] observed that under experimental conditions the number of organisms decreased at a constant rate, the rate at which they were killed varying with different organisms. From these experiments they were unable to detect any destruction or absorption of penicillin by the organisms. Penicillin is not inhibited by serum, tissue extracts or products of tissue breakdown, and in this respect it is superior to the sulfonamide compounds.[11] When the substance was given intravenously, approximately half the material was excreted into the urine, without evidence of renal damage.[12] None was detected in the spinal fluid or the tears.[13] On the basis of present evidence, it appears that the substance should be most useful in the treatment of infections with Staph. aureus, Streptococcus pyogenes, Diplococcus pneumoniae, Neisseria gonorrhoeae and Neisseria intracellularis, as well as organisms associated with gas gangrene. It has no effect on the acid-fast bacilli or the virus of influenza.[8]

Technical difficulties in the preparation of this material have to a large degree retarded the widespread clinical use of penicillin. However, a little more than 20 cases have been reported in which treatment with this substance was successful. These cases have primarily been instances of severe septicemia.[14] However, the Oxford group of workers [4] included 4 cases of ocular infection in their series. A summary of these cases may be interesting in revealing the nature of the ocular conditions and the manner in which penicillin was used.

Case 1.—A woman aged 32 had a history of a corneal ulcer of the left eye for the past four months. This was treated by instillation of colloidal silver, solution of boric acid, merbromin and ultraviolet rays. Under this treatment the ulcer resolved in six weeks. However, three weeks later a similar ulcer developed in the right eye. This was treated along similar lines for six weeks, without improvement. The patient was then admitted to the hospital, and examination showed an infiltrating ulcer of the cornea, located in the inner and upper quadrants of the limbus. There were gross injection of the conjunctiva and considerable corneal opacity. Cultures of material from the eye yielded Staph aureus. Treatment was started with instillation into the eye of a 1:5,000 dilution of sodium penicillin in saline solution every hour by day and every two hours by night. After two days of this treatment there was little visible progress; so continuous application was deemed necessary. A modification of the Bunyan-Stannard bag was made to fit the eye and a 1:5,000 solution of sodium penicillin run into it. (This is the bag that is used in the envelope method of treatment of burns, as reported by Bunyan.[15] No details are given as to the exact method by which the bag was modified to fit the eye and the means by which the lids were kept opened.) After one day of continuous application there was less injection of the conjunctiva and the patient was free from pain for the first time. On the second day the concentration of sodium penicillin in the saline solution was raised to 1:1,000, but this caused slight irritation; so for the next two days a 1:2,500 dilution was used. By the end of the fourth day the eye was greatly improved; the conjunctiva was only slightly injected, and the corneal opacity had almost disappeared. The deep ulcer remained but was considerably smaller. Treatment was then continued with hourly drops of the 1:2,500 solution, and after one day this concentration was increased to 1:500, "therapeutic penicillin," which caused no discomfort. Eight days after the initial use of penicillin, the ulcer no longer stained with fluorescein, but there was still slight injection. Treatment was then continued with drops of a 1:500 solution of sodium penicillin every two hours by day and every four hours by night, but further improvement was slow. After eight days of this treatment the patient had only a slight residual infiltration of the conjunctiva, which cleared up a week later.

Case 2.—A girl aged 19 had an infected cigaret burn of her face of six weeks' duration. A week before admission her left eye became red, swollen and painful. On admission she was found to have impetiginous lesions

7. Hobby, G. L.; Meyer, K., and Chaffee, E.: Activity of Penicillin in Vitro, Proc. Soc. Exper. Biol. & Med. **50**:277-280, 1942. Chain and others.[3] Abraham and others.[4]

8. Robinson, H. J.: Toxicity and Efficacy of Penicillin, J. Pharmacol. & Exper. Therap. **77**:70-79, 1943.

9. Herrell, W. E.: Further Observations on the Clinical Use of Penicillin, Proc. Staff Meet., Mayo Clin. **18**:65-76, 1943.

10. Hobby, G. L.; Meyer, K., and Chaffee, E.: Observations on the Mechanism of Action of Penicillin, Proc. Soc. Exper. Biol. & Med. **50**:281-285, 1942.

11. (*a*) Hobby, G. L.; Meyer, K., and Chaffee, E.: Chemotherapeutic Activity of Penicillin, Proc. Soc. Exper. Biol. & Med. **50**:285-288, 1942. (*b*) Chain and others.[3] (*c*) Abraham and others.[4]

12. (*a*) Herrell, W. E.; Heilman, D. H., and Williams, H. L.: Clinical Use of Penicillin, Proc. Staff Meet., Mayo Clin. **17**:609-616, 1942. (*b*) Hobby, Meyer and Chaffee.[11a]

13. Rammelkamp, C. H., and Keefer, C. S.: The Absorption, Excretion and Distribution of Penicillin, J. Clin. Investigation **22**:425-437, 1943.

14. Abraham and others.[4] Herrell.[9] Herrell and others.[12a]

15. Bunyan, J.: Envelope Method of Treating Burns, Proc. Roy. Soc. Med. **34**:65, 1940.

n both sides of the face. The conjunctiva of the left ye was inflamed and showed a thick mesh of fine vessels; the cornea was clear. The eye bag used in the previous case was filled with a 1:2,500 solution of sodium penicillin, and continuous application was started. On the following day there was less injection, and the eye was not painful. After three days of this treatment the eye was almost normal; treatment was then continued with drops of a 1:500 solution of sodium penicillin every two hours by day and every four hours by night for one day, after which the eye was considered normal.

CASE 3.—A man aged 24 had a foreign body removed from his left eye, after which acute conjunctivitis developed. The condition was treated with a solution of boric acid, zinc lotion and colloidal silver, and the lids were painted with silver nitrate. There was only slight improvement after ten days of this treatment. Treatment with drops of sodium penicillin resulted in rapid improvement and complete relief of pain in two days. This treatment was continued for ten days longer, when healing was complete.

CASE 4.—A woman aged 20 had acute mucopurulent onjunctivitis. The condition was treated with boric cid and zinc lotion, and the lids were painted with lver nitrate. There being no improvement after two ays of this treatment, drops of penicillin were used, nd the eye was regarded as healed in five days.

From these cases one may conclude that penillin resulted in rapid relief of pain and resoluon of inflammation in certain ocular conditions, without any harmful effects on the eye. Penicillin proved to be more effective in the eatment of experimentally produced staphylococcic ulcers of the cornea than a 15 per cent lution of soluble sulfathiazole or a 30 per cent lution of sodium sulfacetimide. Robson and cott[16] obtained staphylococci from human sions which in preliminary tests on rabbit eyes nsistently produced corneal lesions. A dilun of a culture of the organisms thus obtained as injected into the cornea to make a small eb under the epithelium. In each animal, one e was treated with the appropriate chemoerapeutic agent, while the other eye was simirly treated with saline solution. The treatment as first applied one hour after inoculation and as continued hourly for the next forty-eight ours and thereafter at less frequent intervals. 30 per cent solution of sodium sulfacetimide oved more effective than sulfathiazole but not effective as penicillin under these conditions. ese results are not surprising in the light of e observations of some workers[17] that local plication of sodium sulfacetimide in rabbits oduced a greater concentration in the aqueous than sulfathiazole. From these experiments one may conclude, at least experimentally, that the ocular penetration of penicillin is so great that it is more effective than any known sulfonamide compound.

Although the number of cases reported is small in which penicillin has been of value in the treatment of certain ophthalmic conditions, the drug is nevertheless a welcome addition to the limited means of treatment of recalcitrant corneal ulcers.

Roberts and his co-workers[18] extracted another form of penicillin from the culture medium of strains of Penicillium notatum. This substance, which they called penicillin B, is not soluble in organic solvent, in contrast to the original penicillin. It is highly active against gram-positive, as well as gram-negative, organisms. Recent work[19] has shown it to be a protein with an enzymic action, the antibacterial properties of which are attributed to the liberation of hydrogen peroxide as one of the products of its enzymic action. It is relatively stable in its dry state and a great deal more potent than original penicillin; the growth of Staph. aureus is inhibited in a dilution of 1 part in 6,000,000,000. Unfortunately, penicillin B is toxic for mice when injected subcutaneously, as 0.25 mg. causes death in from three to twenty-four hours. However, larger quantities are tolerated when repeated smaller injections are made, an indication that the substance has no cumulative toxicity. At any rate, its potency, stability and apparent polyvalent activity may prove useful clinically, at least for local application in certain ocular conditions.

Dubos[20] isolated a soil bacterium capable of producing a substance which caused lysis of living gram-positive cocci. His discovery was the result of a systematic attempt to discover microorganisms that would attack the living cells of gram-positive cocci. To achieve this end, he used suspensions of living streptococci and staphylococci to which were added the soil mixture, in the hope that they would develop in the soil sample a microbial flora which would be antagonistic to the organisms used. By such methods he was able to isolate a strain of Bacillus brevis, an aerobic, sporulating organism, which pro-

6. Robson, J. M., and Scott, G. I.: Effect of Certain emotherapeutic Agents on Experimental Eye Lesions oduced by Staphylococcus Aureus, Nature, London :581-582, 1942.

7. Robson, J. M., and Scott, G. I.: Local Effectiveof Sodium Sulphacetamide, Brit. M. J. **1**:5-8, 1942. on, H., and Bellows, J. G.: Corneal Penetration of anilamide and Some of Its Derivatives, Arch. Ophth. 34-39 (Jan.) 1942.

18. Roberts, E. C.; Cain, C. K.; Muir, R. D.; Reithel, F. J.; Garby, W. L.; Jones, L. R., and Dorsey, E. A.: Penicillin B: An Antibacterial Substance from Penicillium notatum, J. Biol. Chem. **147**:47-58, 1943.

19. Van Bruggen, J. T.; Reithel, F. J.; Cain, C. K.; Katzman, P. A., and Doisy, E. A.: Penicillin B: Preparation, Purification, and Mode of Action, J. Biol. Chem. **148**:365-378, 1943.

20. Dubos, R. J.: Bactericidal Effect of an Extract of a Soil Bacillus on Gram-Positive Cocci, Proc. Soc. Exper. Biol. & Med. **40**:311-312, 1940.

duced a soluble principle that was extremely toxic to gram-positive bacteria. By means of differential treatments of an autolyzed culture of B. brevis a precipitate, tyrothricin, is obtained. On further extraction of this precipitate with acetone and ether, two crystalline products are obtained.[21] One of these substances has been called gramicidin on account of its selective bacteriostatic and bactericidal effect against gram-positive micro-organisms. The other substance is called tyrocidin because it is rich in the amino acid tyrosine. Tyrothricin[22] is composed of 15 per cent gramicidin and 85 per cent tyrocidin hydrochloride.

In spite of their common origin and the fact that both these substances are polypeptides,[23] gramicidin and tyrocidin differ not only in other chemical properties but in biologic activity. Tyrocidin behaves like a general protoplasmic poison and affects both gram-positive and gram-negative organisms. However, it loses much of its antibacterial activity in the presence of animal tissues, besides being hemolytic.[24] Gramicidin, on the other hand, is completely inactive against gram-negative bacilli, moderately active against meningococci and highly inhibitory to practically all the gram-positive species so far tested, with the exception of the acid-fast bacilli. Gramicidin does not seem to affect the growth and behavior of animal cells in tissue culture,[25] nor is its action decreased by products formed in necrotic tissues.[26] When given intravenously it is very toxic to dogs and mice. It is possible that its hemolytic action may in some way contribute to its toxicity in the blood stream. On the other hand, it appears to exhibit less toxicity when applied locally—for instance, on the mucous membranes. When it is used in open wounds that are fairly deep, there is the danger of absorption and possible hemolytic action Its subcutaneous and intradermal use should abandoned, as such injections produced loc nodules which remained unabsorbed for five six weeks.[28] When it is given orally[29] to dog it has no toxic or therapeutic effect, even aft the administration of quantities one hundred a sixty times the amount capable of killing t tested organisms in vitro. The reason for t oral ineffectiveness of gramicidin is either th it is destroyed by the digestive ferments, as it a polypeptide,or that its action is inhibited fecal material. Its remarkable bacteriostatic a tion is shown by the fact that 0.001 mg. of t substance injected intraperitoneally is sufficie to protect mice against 10,000 fatal doses pneumococci or group A streptococci.

The clinical reports available reveal th gramicidin has been primarily used topically. their 12 cases Herrell and Heilman[27] used t crude substance tyrothricin, which they foun experimentally to have essentially the same bac tericidal effect as that of gramicidin, althoug it may not be as active. Other investigators noted a definite bactericidal effect against strep tococci in cases of bovine mastitis.

The only report of the clinical use of thi substance in ocular therapeutics is that of Bel lows.[31] He noted that a suspension of tyrothrici greater than 0.5 per cent produced considerabl irritation, and even cloudiness, of the corne of rabbits. He was unimpressed with its clinica trial in several cases of acute conjunctiviti Similar observations have been made by Robin son and Molitor,[28] who noted that whe tyrothricin in a 0.5 per cent concentration i saline solution was used in the conjunctiva sac of albino rabbits, there was no evidence o irritation. However, when the dry material wa dusted into the conjunctival sac, there was pro nounced irritation characterized by chemosis and corneal opacity, which were present twenty-fou hours after instillation. The use of an inert powder, barium sulfate, in a similar manner did not produce such effects.

21. Dubos, R. J., and Hotchkiss, R. D.: The Production of Bactericidal Substances by Aerobic Sporulating Bacilli, J. Exper. Med. **73**:629-640, 1941.

22. Hitchkiss, R. D., and Dubos, R. J.: The Isolation of Bactericidal Substances from Cultures of Bacillus Brevis, J. Biol. Chem. **141**:155-162, 1941.

23. Hotchkiss, R. D.: Chemical Nature of Gramicidin and Tyrocidine, J. Biol. Chem. **141**:171-185, 1941. Christensen, H. N.; Edwards, R. R., and Piersme, H. D.: The Composition of Gramicidin and Tyrocidin, ibid. **141**:187-195, 1941.

24. Rammelkamp, H. C., and Weinstein, L.: Hemolytic Effect of Tyrothricin, Proc. Soc. Exper. Biol. & Med. **48**:147-149, 1941.

25. Heilman, D. H., and Herrell, W. E.: Comparative Antibacterial Activity of Penicillin and Gramicidin: Tissue Culture Studies, Proc. Staff Meet., Mayo Clin. **17**:321-327, 1942.

26. Ferraro, W. R.: Comparative in Vitro Effects of Gramicidin and Sulfathiazole on Staphylococcus Aureus, Bull. New York M. Coll., Flower & Fifth Ave. Hosps. **5**:164-173, 1942.

27. Herrell, W. E., and Heilman, D. H.: Expe mental and Clinical Studies on Gramicidin, J. Cl Investigation **20**:583-591, 1941. Rammelkamp and We stein.[24]

28. Robinson, H. J., and Molitor, H.: Some To cological and Pharmacological Properties of Gramici Tyrocidine and Tyrothricin, J. Pharmacol. & Exp Therap. **74**:75-82, 1942.

29. Weinstein, L., and Rammelkamp, C. H.: A Stu of the Effect of Gramicidin Administered by Oral Ro Proc. Soc. Exper. Biol. & Med. **48**:147-149, 1941.

30. Little, R. B.; Dubos, R. J., and Hotchkiss, R. D.: Action of Gramicidin on Streptococci of Bovine Mastitis. Proc. Soc. Exper. Biol. & Med. **44**:444-445, 1940.

31. Bellows, J. G.: Chemotherapy in Ophthalmology. Tr. Am. Acad. Ophth. **47**:19-33, 1942.

In the present state of ignorance, nothing is known of the mode of action of gramicidin. Dubos[32] isolated another bacterial substance from the soil which was capable of decomposing the capsular wall of pneumococci, and in this manner rendered them susceptible to phagocytosis. The action of gramicidin, however, appears to be more subtle and to some extent reversible.[21] For instance, staphylococci which have been "killed" by gramicidin and are unable to grow on meat infusion peptone mediums can be made to grow in the presence of certain tissue components.

Heilman and Herrell[33] showed by the use of tissue culture medium that purified gramicidin and a concentrated preparation of penicillin are of the same order of activity against strains of gram-positive cocci. By the same methods they observed that both substances, besides being bacteriostatic, may be bactericidal under certain conditions. Neither of these substances enhances or inhibits the bactericidal activity of the other. Ferraro[26] observed no advantages in combining sulfathiazole with gramicidin or tyrocidin, since the optimum bactericidal effect was obtained with gramicidin alone.

It is interesting to note that penicillin and gramicidin can be put in a class with the sulfonamide compounds in that they are different from all other antiseptics, which are merely protoplasmic poisons. All three of these substances are primarily bacteriostatic, rather than bactericidal, in their action. Since they do not destroy the respiration of bacteria, one may assume that their bacteriostatic action depends not on the destruction of the entire metabolism of the micro-organisms but on some subtle interference with certain individual biologic reactions.

From the clinical reports published thus far, penicillin appears to be the most potent chemotherapeutic agent known. Its remarkable features include its bacteriostatic action in an amazingly low concentration, its ability to diffuse into infected and dead tissues and its nontoxicity in therapeutic doses. The United States Army[34] has recognized these unusual properties, for the results of its local application in recent preliminary clinical trials have been so encouraging that studies are now being extended to ten general army hospitals. The military requirements will no doubt utilize all available supplies of penicillin; because of this fact, its use should be restricted to infections with local thrombus formation, more particularly to the conditions that are resistant to therapy with the sulfonamide compounds. Its future use in ophthalmology may be limited not only to severe infections of the conjunctiva and cornea but to intraocular infections.

By the present methods of production, it is obvious that penicillin and gramicidin cannot be produced on a scale similar to that of the sulfonamide compounds. However, when a more exact knowledge of their chemical structure, especially of the molecular groups to which they owe their biologic activity, is obtained, the synthetic chemist will have valuable clues for the production of new substances which, it is hoped, may be of greater practical value than either penicillin or gramicidin.

SUMMARY

In a review of the literature on penicillin and gramicidin presented here, their ocular uses, both experimental and clinical, are particularly stressed.

The use of penicillin in clinical ophthalmology has been promising to the limited extent to which it has been reported.

Gramicidin as such has not been reported on as an ocular chemotherapeutic agent, but when it has been used in the form of tyrothricin the results have been disappointing.

Department of Ophthalmology, Cook County Hospital.

32. Dubos, R. J.: The Effect of Specific Agents Extracted from Soil Microorganisms upon Experimental Bacterial Infections, Ann. Int. Med. **13**:2025-2037, 1940.

33. Heilman, D. H., and Herrell, W. E.: Mode of Action of Gramicidin, Proc. Soc. Exper. Biol. & Med. **47**:480-484, 1941; footnote 25.

34. Richards, A. N.: Penicillin, statement released by the Committee on Medical Research, J. A. M. A. **122**: 235-236 (May 22) 1943.

Correspondence

COMPARISON OF OCULAR IMAGERY

To the Editor:—I have read with great interest Dr. Lancaster's comments on my paper entitled "A Comparison of Ocular Imagery," published in the June 1943 issue of the ARCHIVES, and I wish to thank him for his statements and comments. However, he seems to be of the opinion that no instrument save the eikonometer is useful in measuring ocular imagery. As I stated in my original paper, I feel that in their present stage of development neither the eikonometer nor the comparator is adequate for measuring accurately a state of aniseikonia.

The "just noticeable difference" which Dr. Lancaster mentions is well recognized by all ophthalmologists and has been the subject of considerable investigation by various students of the comparator, as well as the eikonometer.

It is unfortunate that the national emergency has interfered with investigation of these two instruments. I am unable at present to accept the eikonometer as the only instrument for comparison of imagery in the two eyes. Dr. Lancaster states that the data obtained by the comparator are of no value. I submit that they are of the greatest value in showing the defects of the instrument.

Efforts are now being expended to overcome the lack of sensitivity of the comparator. As with the eikonometer, work must be done to find a target which gives most sensitivity and yet is not so large that it causes great rotation of the eyeballs.

I am not advocating any one instrument. The fact that in the Army we use the eikonometer for our measurements should indicate our realization of its good points. The fact that we are interested in the development of the comparator should reveal the fact that we do not think the eikonometer a perfect instrument. Again I state, both instruments are in a developmental stage, an embryonic one so to say. It is conceivable that the eikonometer which is eventually used may well be one of revolutionary design.

CAPTAIN HOMER B. FIELD, Medical Corps, Army of the United States.

To the Editor:—I fear I did not make my point sufficiently clear, as I did not wish to be too outspoken. I am not by any means "of the opinion that no instrument save the eikonometer is useful in measuring" aniseikonia, or "ocular imagery," as Captain Field prefers to call it (a better device has long been in use at the Dartmouth Eye Institute), but I was attempting to show that the data given were unscientific. Imagine trying to measure 1 per cent with an instrument on which the subject could not detect 5 or 10 or (in some cases) even 20 per cent; think of expecting a patient to detect a difference of 1/50 inch (0.5 mm.) at 15 feet (457 cm.) and try to conceive of an ophthalmologist's advocating an instrument for measurement of heterophoria which showed systematically a tendency to convergence on his looking into the machine, as the readings for all esophorias were too large and those for most exophorias were too small, to say nothing of the presence of right hyperphoria in 18 of 25 subjects with average vision.

WALTER B. LANCASTER, M.D., Boston.

520 Commonwealth Avenue.

OCULAR OCCLUDERS

To the Editor:—The advantageous use of monocular occlusion for long periods for both diagnostic and therapeutic purposes has been established. In a recent report from the Dartmouth Eye Institute the remarkable benefits to be derived from such prolonged monocular occlusion are detailed. In a number of cases permanent monocular occlusion was found to be the only way to relieve intolerable ocular distress. In over 50 per cent of a series of 80 cases relief was obtained during occlusion and with the prescription obtained after the period of occlusion. The great problem is how to provide an occluder which will not be disfiguring. Monocular occlusion would certainly be much more widely practiced if it were possible to do so with an inconspicuous occluder. An opaque contact lens is probably best, but its use is not always feasible.

The real purpose of occlusion, it seems to me, is to prevent binocular fixation of the object of attention. All the difficulties incident to binocular vision are due to the desire and associated effort to fuse or unify the two macular images. When such fusion has been made impossible or undesirable, the difficulties incident to bimacular vision vanish. The displacement and distortion tests employed in the measurements employ the phoria principle. One eye fixates the target while the other eye, whether or not it ignores the distorted or displaced image, makes no effort to fuse it with the macular image of the fixing eye. In a case of manifest strabismus, for the same reason, there are no visual discomforts which can be attributed to the use of both eyes because there is no bimacular vision. But the deviated eye does not ignore everything in its field of vision.

By employment of the principles of the phoria tests one can eliminate bimacular vision by merely displacing and/or distorting the image in one eye

o such an extent that bimacular vision is neither lesirable nor possible. A clear lens made up on his principle would look much like any other ens in an ordinary pair of spectacles. A similar ens which has been used to avoid annoying liplopia after cataract extraction was recently lescribed by Mr. Edward J. Boyes in *Guildcraft* for April-May 1943. Such a lens also gives the patient some field vision on the side of the 'occluded" eye.

The proper selection of the best lens to be used will tax the ingenuity of both the physician and the optician. The "occluding" lens should be as light as possible and match as nearly as possible the lens worn by the other eye. It may be a sphere, a cylinder or a compound plus or minus sphere and cylinder, all combined with a prism of the least strength necessary to eliminate fusion and annoying diplopia. Probably a strong cross cylinder ground as such or as a spherocylinder or as a toric lens on one or both sides can be made to match most ordinary lenses and to produce sufficient distortion and displacement of the unwanted image. If the plus cylinder is placed at axis 180, it may be possible to introduce sufficient decentration for a prism base up or base down.

Since the critical area of central vision employs only a small section of the lens, probably at most a disk about 20 mm. in diameter, the "occluding" lens may also be made lenticular. The central aiea would carry the distorting and displacing power, and the rest of the lens would allow for peripheral field vision. Finally, when an actual occluding lens must be used, it is sufficient to frost the central area of the lens. I believe, however, that a judicious combination of sphere and/or cylinder and/or prism in a fully clear lens will always accomplish the purpose of monocular "occlusion" with a minimum of annoyance to the patient.

Joseph I. Pascal, M.D., New York.

37 West Ninety-Seventh Street.

CORNEAL TRANSPLANTATION

To the Editor:—In the January 1944 issue of the Archives, page 118, Dr. Olga Sitchevska reviewed a book entitled "Corneal Transplantation with Fresh, Preserved and Fixed Material," by O. I. Shershewskaya.

Her comment that my only operation using fixed material was unsuccessful apparently derived from the Russian original. I should appreciate having this error corrected in the Archives.

The case in question was briefly described in Albrecht von Graefe's *Archiv für Ophthalmologie* **107**: 454, 1922. The last paragraph on this page states that the transplantation of a disk previously fixed in formaldehyde had been performed for tectonic, not for optic, purposes: The intention was to cover a fistula in a case of total corneal leukoma, and the transplant took in spite of having been preserved in formaldehyde for eight weeks prior to the operation. Despite the expectedly poor visual result, the outcome was entirely satisfactory in that the transplant finally closed a fistula which had not responded to other treatments.

K. W. Ascher, M.D., Cincinnati.

2508 Auburn Avenue.

Obituaries

PROF. ALFRED VOGT

1879-1943

For those ophthalmologists who were not personally acquainted with Dr. Vogt, the news of his death on Dec. 10, 1943 may have been a surprise. Until recently they knew him as an active and productive scientist and writer. His close friends, however, were more amazed that he was able to carry on as long as he did. In 1939, for his sixtieth birthday, his friends and former assistants presented him with a "Festschrift"[1] containing over ninety papers, written in several languages and by people from all over the world. As it was already known that Dr. Vogt suffered from a severe vascular disease, his friends were all happy that this demonstration of appreciation of the master's work came in time for him to enjoy it. For the last four years only an almost superhuman energy, combined with complete devotion to his task, enabled him to continue his work.

In evaluating an outstanding personality like Alfred Vogt's, one always feels inclined to comparisons with figures of the past. Vogt's work and career indeed remind one in many ways of those searchers and fighters of the early days of modern medicine. Like Robert Koch, for instance, Vogt made some of his fundamental discoveries far away from the country's institutes designed and equipped for research. While practicing ophthalmology in a provincial town, his imaginative mind led him to fundamental studies and experiments. His academic career likewise was unusual. He did not spend decades at some institution, repeating his master's voice, in order to slip finally into some position, as is done usually. He was called to head an ophthalmic institute in a university directly out of his practical position, without having climbed the academic ladder step by step.

Alfred Vogt was born in 1879 on a farm near Aarau, Switzerland, his father being a school teacher and farmer at the same time. His inclination for the natural sciences became evident when, still a boy, he assembled an unusually complete collection of butterflies. He also was interested in history and was particularly impressed by the struggle for freedom of the old Swiss. Indeed, he continued to love his country and its democratic institutions all his life. After graduation from the University of Basel he got his ophthalmologic training mainly at the Ophthalmic Institute of the University of Basel, at this time directed by Mellinger. He then established himself as specialist in ophthalmology at Aarau and became head of the department of ophthalmology in the cantonal hospital of that town. Having been one of the first to recognize the importance of Gullstrand's ingenious invention of the slit lamp for study of the morphology and pathology of the eye, he improved this instrument and put it to work with all the thoroughness, endurance and imagination characteristic of him. It was then, too, that Vogt discovered the surprising result of using red-free light for ophthalmoscopy. He could prove, for instance, that the macula lutea in the living eye was really yellow, bringing to a conclusion an age-old controversy. His discoveries, however, were passionately questioned by the recognized experts in the respective fields of ophthalmology. C. von Hess stubbornly stuck to his description of the morphology and the pathogenesis of the senile cataract, which was in disagreement with Vogt's observations. But although von Hess, who was one of my venerated teachers, was then a leading ophthalmologist, he proved to be wrong, having become the victim of an experimental setup which was much inferior to Vogt's slit lamp. Gullstrand passionately denied the presence of any color in the macula lutea, defending his own theory of a phenomenon of contrast. But he, too, proved to be wrong, as every one using Vogt's new light could really see the yellow color of the macula. These victories over two of the most prominent representatives of contemporary ophthalmology made Vogt appear in the spotlight almost overnight.

In 1918 he was appointed professor of ophthalmology and director of the Ophthalmic Institute of the University of Basel. In 1923 he received and accepted a call to direct the University Ophthalmic Institute of Zurich, which was a great honor in view of the high tradition of this institute, men like Horner and Haab having been connected with it. As professor of ophthalmology, Vogt soon became one of the most prominent members of the faculty. He

1. The "Festschrift" also contains a complete chronologic list of Professor Vogt's contributions.

emained in this position until his resignation, few months before his death.

The work accomplished by Vogt during the wenty years in Zurich is equally impressive in olume and in quality. Although he concentrated n some special subjects, his publications cover lmost the whole field of theoretic and practical phthalmology. It will be possible to mention ut a few of his major contributions here.

Vogt's "Atlas of the Slitlamp Microscopy of he Living Eye" (Berlin, J. Springer, 1921) is robably his best known work in America. Before I left Switzerland, in 1941, for a study rip to this country, Vogt seemed for a while to

ALFRED VOGT, M.D.
1879-1943
(Festschrift für Herrn Professor Dr. A. Vogt, Klin. Monatsbl. f. Augenh., October-November 1939, vol. 103.)

be inclined to join me, as many invitations had already reached him. Finally, however, he decided to stay in order to complete the third volume of his "Atlas." He must have felt that the days of work would come to an end and that he could not afford to waste any time. After the volume had been printed and published in Switzerland, he sent me one of the first copies and asked me to make arrangements for an English edition. There is hope that this atlas, equally outstanding for its text and for the accuracy of the illustrations, will be made available to the English-speaking world in the near future. As a matter of fact, many American ophthalmologists received their first training with the slit lamp from Vogt, while attending his courses in Zurich.

In connection with exhaustive clinical and pathologic studies of the so-called glass blower cataract, Vogt proved by numerous ingenious experiments that infra-red radiation may cause cataract in rabbits, as he thought, partly because of a special affinity of the lens fibers for this category of radiation and partly because of the heat produced when the rays strike the pigmented iris and the ciliary body. Thus he was able to give a satisfactory explanation of this industrial disease.

Having been one of the first to accept Gonin's theory and technic of the surgical treatment of the detachment of the retina, he tried it out on a large number of patients, improving the technic and summarizing his experience in the book entitled "Die operative Therapie und die Pathogenese der Netzhautablosung" (Stuttgart, Germany, Ferdinand Enke, 1936). The study of this book is of tremendous value for any one engaging in the surgical treatment of the detached retina. Out of the experience with perforating diathermy in the operation of the retinal detachment Vogt developed what he called the "cyclodiathermy puncture" of the ciliary region as a measure in certain complicated cases of glaucoma. He also devised a special instrument for this operation.

Important work was done by Vogt in the field of heredity. He produced countless cases and pedigrees of various diseases now recognized to be of hereditary nature. Most of this work, of course, concerned diseases of the eye, but having at his command an extensive knowledge of general natural science, Vogt often engaged in more general problems of human pathology, dental caries being one of them. The most original contribution in the field of heredity is the study of senile changes in identical twins, which he carried out during the last few years. It appeared that the eyes of identical twins are alike to a large extent, including even minor details, and special emphasis was given the fact that senile cataract not only appeared at the same period of life but was of the same morphologic type in each twin, although they had lived in entirely different environs. These observations have been published in part by Vogt and his assistants in the *Archiv der Julius Klaus Stiftung für Vererbungsforschung, Sozialanthropologie und Rassenhygiene,* in 1939, and now constitute one of the most interesting parts of the third volume of the "Atlas," published in 1942.

A great writer himself, Vogt belonged to the editorial staff of a number of ophthalmologic periodicals, the *Klinische Monatsblätter für Augenheilkunde, Albrecht von Graefes Archiv für Ophthalmologie* and *Zeitschrift für Augenheilkunde* being probably the ones which profited most from his contributions. He also was a member of a number of scientific societies in various countries, but he was most devoted to the Swiss ophthalmologic society, of which he was one of the founders and a past president. Many of his discoveries have been reported first at its annual meetings. He also made an endowment to this society to induce the award of a prize for the writer of the best paper each year. This endowment was made in memory of his only son, who died tragically in an avalanche accident in the Swiss Alps. Vogt's keen interest in the Swiss ophthalmologic society naturally had a tremendously stimulating effect, which undoubtedly accounts in great part for the unusually high standard of the contributions made by this numerically small group.

Vogt's work and personality earned highest public appreciation on several occasions. A call from the University of Munich, second only to the University of Berlin, undoubtedly was a great honor. But Vogt could not make up his mind to accept it, and I know he never regretted having remained in his independent position in Switzerland. He was awarded the Donders medal and recently, in 1942, the golden Gullstrand medal, which represent the highest distinction any ophthalmologist can receive.

Besides his work as a scientist, writer and teacher, Vogt was engaged in an enormous private practice, and it is hardly exaggerated to say that he had become the most famous ophthalmologist of the European continent. Many prominent people were among his patients, although not all the sensational stories reported by the newspapers were true. Vogt himself, more amused than embarrassed, explained to me how some of these stories originated from simple confusion. There are always legends being built up around a famous name. But all this fame did not prevent Dr. Vogt from giving his full attention and all of his precious time to a poor patient of the ward if his personal intervention was indicated, as I myself witnessed in many instances.

It is obvious that so much work could not be done without sacrifices in private life. Although he was a devoted husband and father, Vogt's family, his wife and two lovely daughters, who remained after his only son's tragic death, were not given the privilege of enjoying him as much as they desired and deserved. I should even say that not all that work for the benefit of humanity would have been possible without the unselfish attitude of Mrs. Vogt, who was sincerely interested in her husband's work and anxious to manage so that his social life caused the least possible interference. There was, also, little time left for hobbies, an occasional fishing trip and the collection of paintings being those Vogt enjoyed most.

Many people thought Vogt was short, and even rude, at times. It is true that he did not like many words when it was, in his opinion simply a matter of stating the facts. He was frank and would not hesitate to say exactly what he thought to patients, to colleagues or to anybody. But he was not unkind, and he certainly was sincere. When he called some one his friend, he meant it and was ready to stand by at any time. Those who had the privilege of knowing more intimately this unusually strong and interesting personality not only enjoyed his always spirited conversation but were often touched when they recognized that, however hard the shell, it sheltered a loving and sympathetic heart.

Alfred Vogt will always have a place among the great physicians and scientists of all time. To ophthalmology few have contributed as much as he did. He was equally as capable of conceiving a new idea as of assembling minute details. This makes his work unusually complete. An extremely hard worker and a strong and upright character, he was the real personification of that rough mountain country from which he originated.

FREDERICK W. STOCKER.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Aqueous Humor

DIFFERENCES OF TENSION IN THE CHAMBERS OF THE EYE: REPORT OF A CASE. A. LUZSA, Klin. Monatsbl. f. Augenh. **106:** 422 (April) 1941.

The author discusses the unsolved problem of the production, circulation and drainage of aqueous humor. The theories of Leber and Hamburger are given special consideration. Luzsa had an opportunity to study this problem in the case of a boy aged 7 both of whose eyes were smaller than normal, the corneal diameters being 9 mm. in both principal meridians. Persistent hyaloid membranes were present in both eyes, the fundi of which were otherwise normal. The right eye showed a congenital, incomplete coloboma in the lower portion of the iris, located slightly nasal to the median line. The pigment layer and the reaction of the pupil were normal. Both eyes were hyperopic, and the left eye manifested amblyopia and an internal strabismus. The left eye presented a dark brown, bullous prominence in the lower portion of the iris, slightly nasal to the median line and about 3 mm. in diameter.

The bulla changed its shape and size, extending when the patient looked at a distance and collapsing on accommodation for near vision. The bulla collapsed with pressure on any portion of the cornea, extending again on release of the pressure. This procedure could be repeated in swift succession. The bulla collapsed occasionally when the child batted his lids. It emptied slowly when he was asked to look gradually at a distance and became distended when he looked at a distance of 75 cm.

Luzsa thinks that the bulla was caused by a small area of hypoplasia in the iris, followed by protrusion of the pigment layer. Its extension was due to afflux of aqueous humor into the posterior chamber. This process is indicative of a difference in pressure between the anterior and the posterior chamber, the pressure being alternately higher in one and in the other. The difference occurred simultaneously with the change in the form of the lens and its position during accommodation. Contraction and dilatation of the pupil had no influence on the difference of pressure in the chambers.

No information regarding the circulation of the aqueous humor could be gained from this case.

K. L. STOLL.

Congenital Anomalies

FIBROBLASTIC OVERGROWTH OF PERSISTENT TUNICA VASCULOSA LENTIS IN INFANTS BORN PREMATURELY. T. L. TERRY, Am. J. Ophth. **25:** 1409 (Dec.) 1942.

This is the third of a series of studies on the development and regression of the hyaloid artery and the tunica vasculosa lentis. The material used consisted in serial sections of eyes from more than 50 human fetuses, representing many stages of development. The eyes of fetal and newborn animals, including the cat, rat, pig and opossum, were also studied. The observations and conclusions are summarized.

W. S. REESE.

ARACHNODACTYLY (MARFAN'S SYNDROME) A. A. BARRON, North Carolina M. J. **3:** 353 (July) 1942.

Barron reports on a family, several members of which had arachnodactyly. The mother and 6 of her children showed the characteristic elongated bony structure. Four of the siblings had ectopia lentis. Of these 4, 1 had a left lateral curvature of the lumbar portion of the spine, while another had had two acute attacks of lymphocytic meningitis and chronic symptoms which seemed to indicate involvement of the central nervous system. There is no proof either that this simultaneous occurrence of meningeal and arachnodactylous symptoms was a coincidence or that the two chronic conditions were linked in close association. The article is illustrated.

W. ZENTMAYER.

Cornea and Sclera

SULFADIAZINE IONTOPHORESIS IN PYOCYANEUS INFECTION OF RABBIT CORNEA. L. VON SALLMANN, Am. J. Ophth. **25:** 1292 (Nov.) 1942.

In experiments on rabbits von Sallmann observed that iontophoretic administration of sulfonamide compounds achieved higher concentrations in the anterior segment of the eye than other clinical methods, sulfadiazine entering in greater amounts than the other sulfonamide drugs studied. Sodium sulfadiazine so used in a case of infection of the rabbit cornea with Bacillus pyocyaneus gave results superior to other local methods and to general treatment. These good results were enhanced by oral use of sulfadiazine. The most favorable treatment of keratitis of this type in rabbits was a combined method of iontophoretic administration of sodium

sulfadiazine and local and oral use of the powder. These observations were confirmed by the results of treatment of 2 patients suffering from corneal ulcers due to infection with B. pyocyaneus.

W. S. Reese.

A Case of Bowen's Disease of the Cornea. G. Wise, Am. J. Ophth. **26:** 167 (Feb.) 1943.

Wise discusses Bowen's disease from the clinical, pathologic and metastatic standpoints. He reports a case of the disease in an Italian aged 62, in whose right eye there were three distinct small, fleshy, pink masses, located at 3, 12 and 9 o'clock on the limbus. These were freshly movable and unattached to the limbus and were fed by dilated, somewhat tortuous, vessels. The cornea was covered with an opaque, uneven, thickened tissue, which connected with each lesion in the limbus. The mass was excised, and a diagnosis of intraepithelial epithelioma was made.

W. S. Reese.

The Treatment of Herpetic and Dendritic Ulcers. F. O. Schwartz, Am. J. Ophth. **26:** 394 (April) 1943.

Schwartz reports cases of herpetic and dendritic ulcers of the cornea. In all cases foci of infection were present in the sinuses, tonsils or teeth, and there was an undoubted relation between these foci and the corneal ulcers; all the corneal lesions resisted treatment and made no definite progress until these foci were removed. The author concludes that an unidentified virus, which may have its origin in the focus of infection, should be considered an etiologic factor in the production of herpetic and dendritic keratitis.

W. Zentmayer.

Fungous Diseases of the Cornea: Report of Cases. A. Fazakas, Klin. Monatsbl. f. Augenh. **106:** 56 (Jan.) 1941.

Fazakas noted various types of fungi in 25.65 per cent of healthy eyes and in 37.08 per cent of diseased eyes. He concludes that the cornea, the conjunctiva, the lacrimal apparatus and the palpebral margin in the region of the meibomian glands offer better nutrition to fungi in diseased than in normal conditions. He observed about two dozen forms of fungi, which retarded recovery, for instance, from trachomatous and eczematous pannus. The fungus changed the picture of the initial disease in some instances, as in a case of dentritic keratitis and in several cases of trachoma, inclusion blenorrhea and acute and chronic simple conjunctivitis. Most keratomycoses are produced by Aspergillus; the fungus produces ulcers, or nodules, occasionally appearing on different portions of the cornea. In 1 case of infection with Aspergillus flavus there were several recurrences with severe keratitis and iritis, followed by glaucoma. The decrease in intraocular tension after paracentesis of the anterior chamber was maintained only as long as the corneal wound remained open. The escaping aqueous failed to dislodge the fungus colonies in the anterior chamber. Final recovery was obtained by repeated paracenteses and flushing the anterior chamber with solution of iodides.

K. L. Stoll.

General Diseases

The Diagnosis of Ocular Syphilis. B. F. Payne, Am. J. Ophth. **26:** 266 (March) 1943.

Payne discusses the diagnosis of syphilis and emphasizes the importance of early detection of the disease. He cites other diseases with which the Wassermann and other serologic tests give positive reaction. He refers briefly to treatment, suggesting that here the ophthalmologist should play the role of an umpire and confine his attention to the eye.

W. S. Reese.

Arteritis of the Temporal Vessels Associated with Loss of Vision. R. H. Johnson, R. D. Harley and B. T. Horton, Am. J. Ophth. **26:** 147 (Feb.) 1943.

The authors report 3 cases of loss of vision due to retinal or retrobulbar vascular accidents associated with arteritis of the temporal vessels. The authors believe that the arteritis was more extensive than could be detected on careful physical examination. Microscopic examination of resected temporal vessels for the most part indicated a chronic inflammatory process. None of the patients has died.

W. S. Reese.

Ocular Findings in a Case of Periarteritis Nodosa. I. E. Gaynon and M. K. Asbury, Am. J. Ophth. **26:** 1072 (Oct.) 1943.

In a case of periarteritis nodosa autopsy revealed advanced generalized arteriosclerosis with terminal focal arteriolar sclerosis, focal syphilitic arteriolitis and focal periarteritis nodosa. In the choroid the predominating vascular lesion was arteriosclerosis with terminal necrosis. A few vessels in both the retina and the choroid showed inflammatory changes suggesting in some instances syphilitic arteriolitis and in others early periarteritis nodosa. Failing vision due to a pathologic condition of the retina typical of malignant hypertension was the first symptom.

W. Zentmayer.

Glaucoma

Evaluation of Glaucoma Operations. B. F. Payne, Am. J. Ophth. **25:** 1474 (Dec.) 1942.

From a study of 100 enucleated eyeballs, Payne reached the following conclusions:

"A satisfactory evaluation of operations for glaucoma would appear to be hopeless in the face

of the cases . . . described. From the findings it would seem that any type of surgical procedure must be doomed to failure. It should be remembered, however, that these specimens represent failures, and despite the fact that there is no satisfactory operation for glaucoma there is some hope in the choice of surgical procedure. In reviewing the material for this paper, which was collected over a period of 10 years, it was noted that most enucleations followed paracentesis, posterior sclerotomy, and iridectomy. The number of specimens submitted after iris-inclusion operations, corneosclerectomy, and trephining amounted to less than 15 per cent of the total. From the viewpoint of the pathologist it seems that some form of corneosclerectomy is the operation of choice."

W. S. Reese.

The Effect of Mydriatics upon the Intraocular Pressure in So-Called Primary Wide-Angle Glaucoma. P. C. Kronfeld, H. I. McGarry and H. E. Smith, Am. J. Ophth. **26:** 245 (March) 1943.

From their tests on human eyes, the authors onclude that the response to mydriatics of early o-called primary wide-angled glaucoma is as a ule less constant than the response to the drinkng test of Marx and Schmidt and that the latter est is therefore of greater diagnostic value.

W. S. Reese.

Hygiene, Sociology, Education and History

The Story of the Red Cross Institute for the Blind (1918-1925) in Relation to the Present Problem of the War Blinded. A. C. Woods, Am. J. Ophth. **26:** 1011 (Oct.) 1943.

The Red Cross Institute for the Blind, organized first as General Hospital no. 7, but generally known as the Evergreen School for the Blind, was the agency established during World War I for the training and rehabilitation of members of the armed forces who became blind. In Woods's personal files are the records of 325 cases, which represent the total number of men trained at this school from March 23, 1920 until the close of the school in June 1925.

A review of the 325 cases shows that, on the basis of the ocular lesion, they may be classified as follows: trauma, 106 cases; disease of the optic nerve 66 cases; hysterical amblyopia, 27 cases; atrophic choroiditis, 17 cases; retinitis pigmentosa, 14 cases; amblyopia due to systemic disease, 12 cases; errors of refraction, 14 cases; injuries due to war gas, 12 cases; cataract, 12 cases; uveitis with secondary cataract, 8 cases; superficial keratitis, 9 cases; interstitial keratitis, 8 cases; trachoma, 5 cases; amblyopia due to cortical injury, 4 cases; detachment of the retina, 4 cases; glaucoma, 3 cases; superficial retinitis, 2 cases, and keratoconus and nystagmus, 1 case each.

Woods analyzes each group. The latter part of the article is devoted to a thoughtful consideration of questions concerning the men blinded during the present war but does not lend itself to abstraction.

W. Zentmayer.

A Summary of Findings at the Eye Examination of Preparatory-School Boys. A. E. Sloane and J. R. Gallagher, Am. J. Ophth. **26:** 1076 (Oct.) 1943.

The authors provide the following summary:

"1. Findings in various parts of an eye examination of a group of 1,009 preparatory school boys are given.

"2. The data indicate the importance of adequate screening eye examinations as a part of any health program involving adolescents.

"3. The desirability of including tests of hypermetropia and heterophoria as well as of visual acuity in any screening examination is shown.

"4. Questions regarding blurred vision, red eyes, and headaches are best asked by a physician: the evaluation of such symptoms will not be helpful unless the history has been carefully taken.

"5. There are at present no valid reasons for omitting annual eye tests even among children of the more privileged economic group.

"6. The Snellen test is inadequate for the selection of all children in need of a careful eye examination.

"7. The recommendation, on the basis of screening tests, for a further careful examination is better made by a physician after a consideration of all of the findings than by lay persons relying on set quantitative measurements alone."

W. Zentmayer.

Injuries

Eye Surgery in War Time. E. Hartman, Am. J. Ophth. **25:** 1448 (Dec.) 1942.

The paper is based principally on the author's personal experience and on Duverger and Velter's book, "Ophthalmologie de guerre." The various injuries resulting from war and their treatment are outlined.

W. S. Reese.

Concerning Lagrange's Law of Indirect Ocular War Injuries. P. S. Soudakoff, Am. J. Ophth. **26:** 293 (March) 1943.

From a study of reported cases, Soudakoff concludes as follows:

"Analysis of the cases of indirect war injuries to the eye communicated by various authors discloses the existence of a distinct relationship between ocular lesions and injuries of the facial bones. The presence of the fracture of the facial bones as well as the fracture of the anterior or posterior orbital wall predicts definite lesion of

the membranes of the eye, or injury to the optic nerve, according to the laws formulated by Lagrange.

"The observations of the indirect injuries of the eye during the present war will give ample opportunity for American ophthalmologists to verify the correctness of Lagrange's deduction and to modify his law according to new findings."

W. S. Reese.

Nonsurgical Aspect of Ocular Injuries. F. C. Cordes, Am. J. Ophth. 26: 1062 (Oct.) 1943.

The discussion of ocular injuries is based on knowledge gained during World War I, in civilian practice and from the reports from abroad based on experiences in Poland, Barcelona, Dunkirk, Coventry, London and the front lines.

Cordes stresses the following fundamental principles that should be kept in mind in the care of ocular injuries in war time.

"1. Penetrating wounds of the globe, iris prolapse, and lid injury require immediate surgical care if the proper facilities are available. If not, the wounds should be cleaned, a dressing applied, and the patient sent to a base where proper facilities are available. In the event of a lid injury a moist dressing is indicated. In cleaning up lid injuries débridement technique used in other wounds would be ruinous to the lids and conjunctiva where every millimeter of tissue must be saved.

"2. As to foreign bodies of the cornea and globe, experience indicates that it is best not to interfere until the patient has recovered from shock and until the foreign bodies can be removed under favorable circumstances. It is also well to remember that minute foreign bodies of the cornea are often spontaneously extruded during the first 24 hours.

"3. In cases of thermal burns of the cornea the routine, continued use of anesthetics is to be avoided, as any of the anesthetics interfere with the healing of the cornea. In general it has been found that unless there is some definite indication for the local use of drugs, the eyes recover from injury more rapidly if these are not employed.

"4. War-gas burns of the eyes or exposure to war gas requires immediate attention. The most effective universal treatment, irrespective of the type of gas, or in the event of a mixture of gases, would appear to be that based on an alkaline hydrolysis by the use of approximately 2 per cent sodium bicarbonate. This can be simply made by dissolving a teaspoonful of baking soda in a glass of water."

W. Zentmayer.

Lids

Modified Ewing Operation for Cicatrical Entropion. J. E. Smith and A. A. Siniscal, Am. J. Ophth. 26: 382 (April) 1943.

The authors have used a modified Ewing operation for cicatricial entropion in over 500 patients, with recurrence of the incurvation in only 0.5 to 1 per cent of the series. The method provides a wide range of application and can be effective either to the upper or to the lower lid.

The various steps of the operation are well illustrated.

W. Zentmayer.

A Combined Ptosis Operation. O. H. Ellis, Am. J. Ophth. 26: 1048 (Oct.) 1943.

A combined operation for the correction of ptosis is described. The method utilizes a strip of the tendon of the superior rectus muscle, the transplant being allowed to heal in the desired position in the upper lid without tension, as a result of the placement of Pagenstecher sutures. The procedure is based on firm surgical principles and is indicated in cases in which there is good action of the superior rectus muscle. The steps of the operation are clearly illustrated in the article.

W. Zentmayer.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

FRANK C. KEIL, M.D., *Chairman*

WILLIS S. KNIGHTON, M.D., *Secretary*

Dec. 20, 1943

Transscleral Removal of Intraocular Foreign Body with Aid of the Berman Locator. DR. HENRY MINSKY.

This article will be published in a later issue of the ARCHIVES.

Foreign Body in the Lens with Formation of Cataract: Method of Extraction. DR. A. RUSSELL SHERMAN, Newark, N. J.

A man aged 31 was struck in the right eye ith a piece of steel. Examination of the eye x weeks later revealed a perforating scar in le cornea, a hole in the underlying iris and a osterior subcapsular opacity in the lens. A oreign body lay in the anterior part of the lens. 'ision was 20/40.

Within two months the lens swelled and re-uced vision to perception of hand movements; ater iron pigment surrounded the foreign body, ut there was no siderosis.

Operation was performed about eight months fter the accident. A keratome was introduced hrough the upper part of the cornea and was arried into the lens. The foreign body was re-noved with a hand magnet and the cortex of the ens washed out. Final corrected vision was 20/20.

This case is reported to illustrate a satisfactory nethod of treating a patient with a magnetic oreign body in the lens. Removal of the foreign body before a cataract has formed may produce a cataract and require an extraction at a time when he eye is not in the most favorable condition or operation. It is not advisable to attempt to lraw the foreign body through the lens capsule, ince the resistance to the passage of the body is onsiderable and the lens may be dislocated. It s obvious that the eye must be observed at in-ervals of a few weeks for evidence of siderosis. The probability of uveitis is not great.

Injury to the Ciliary Body Without Iridocyclitis. DR. A. RUSSELL SHERMAN, Newark, N. J.

A man aged 48 was struck in the right eye by a metal pin from a drill press. A roentgenogram did not reveal any foreign body. The wound in the eye extended from the limbus 2 mm. into the cornea and 5 mm. into the sclera, through which the iris, ciliary body and vitreous protruded. This prolapsed tissue was excised; the scleral wound was closed with a suture near the limbus, and the conjunctiva was sutured. Both eyes were covered. Large doses of sulfadiazine were given by mouth, and the eye was not dressed for four days, when there was only slight redness. Eight days after the injury the vitreous was clear and the fundus was seen clearly. The patient was discharged from the hospital.

Three days later there was a large hemorrhage in the vitreous, and no fundus reflex was obtained. Two months later a slight fundus reflex, was visible, and the eye gradually lost its redness and sense of irritation.

This case, in which the ciliary body suffered not only an incision but a partial excision, is reported to emphasize that injury to the ciliary body is not synonymous with loss of the eye, much less with sympathetic ophthalmitis. One need not fear sympathetic inflammation during the first two or three weeks, or for a much longer period, if the fellow eye is kept under frequent observation with a slit lamp. Experience indicates that an eye which during the first few weeks after injury shows progressive lessening of the inflammatory reaction retains its light projection and does not become soft, does not constitute a danger and can usually be preserved, often with useful vision.

Detachment of the Retina Resulting from Traction Exerted by an Intraocular Foreign Body. DR. A. RUSSELL SHERMAN, Newark, N. J.

A man aged 28 was struck in the right eye by a particle from a hammer. There were a small wound of the central part of the lower lid margin and a wound of the conjunctiva just below the limbus. Blood was observed in the vitreous inferiorly, and a detachment of the retina above supported a foreign body, as in a hammock. Vision was 1/200, and there was contraction of the visual field, corresponding to the detachment and to the blood in the vitreous.

The tendon of the superior rectus muscle was severed and reflected upward, together with the conjunctiva and Tenon's capsule. The foreign body, measuring 2 by 2 by 3 mm., was removed with a hand magnet through a scleral incision 3 mm. long, above the cornea and temporal to the muscle. Electrocoagulation was applied through the exposed sclera with the Gradle electrode. A 2 mm. trephine opening was made in the sclera as far back as possible, and the choroid was perforated through this opening with a lacrimal punctum dilator.

During postoperative convalescence there was no evidence of reattachment and no fundus reflex was seen. The tension was too low to register on the tonometer. Although the eye had been white a month after the operation, it became red and painful two weeks later and was enucleated.

Apparently this foreign body, having perforated the globe below, passed upward through the *vitreous, perforating the retina above. It then* dropped downward dragging the retina with it. The detachment of the retina, resulting apparently from the pull of gravity on the foreign body, calls attention to the possibility of the production of such a detachment when a foreign body which has lodged between the retina and the sclera is removed by the anterior route. The operator is just as likely to produce a detachment of the retina by the latter procedure as by removal of the foreign body through a posterior incision.

Management of Industrial Injuries of the Eye. Dr. Elbert S. Sherman, Newark, N. J.

This paper will be published in full in a later issue of the Archives.

Suggested Revisions in the New York State Compensation Laws. Dr. Albert C. Snell Sr., Rochester, N. Y.

Management of Corneal Lacerations. Dr. Albert C. Snell Jr., Baltimore.

An analysis of 172 selected cases of perforating ocular injuries was made in an effort to determine the influence on the final outcome of the various possible complications. The following conclusions were reached:

1. With corneal lacerations less than 8 mm. long the length of the laceration in itself did not influence the chances for recovery.

2. Prolapse of the iris provided protection against intraocular infection.

3. The incidence of intraocular infection complicating perforating injury was 15 per cent and was not materially reduced by treatment with the sulfonamide compounds.

4. Minor intraocular hemorrhage had no effect on the prognosis, but severe intraocular hemorrhage was devastating.

5. Damage to the lens influenced the prognosis adversely, since it favored the development of intraocular infection and uveitis.

6. Results achieved in the repair of corneal lacerations with a conjunctival flap appeared to be only slightly less satisfactory than the use of direct corneal sutures.

Location of a Foreign Body in the Eye with a Contact Lens. Dr. Raymond L. Pfeiffer

DISCUSSION

Dr. A. Russell Sherman, Newark, N. J.: I should like to report on an additional aid in the extraction of foreign bodies which have been localized by Dr. Pfeiffer's method. It is a ring, devised by Guist, to determine the external site of approach to a retinal tear in cases of detachment. The ring, which is marked at 10 degree intervals, rests on the limbus. A soft metal arm is held at the center of the ring by a thumb screw and can be revolved like the hand of a clock, so that it points along any desired meridian of the cornea, as indicated by the markings on the ring. Before the ring is applied, the arm is cut to the right length so that, as it extends beyond the limbus, its free end will lie over the intraocular foreign body. The ring can be left in position until the sclera is exposed, or it can be reapplied afterward, so that the sclera can be marked directly over the foreign body. I have used the ring in 4 cases in which the intraocular foreign body was localized by the contact lens method. In each case the foreign body was observed directly under the external mark on the sclera.

Book Reviews

An Introduction to Clinical Perimetry. By H. M. Traquair, M.D., F.R.C.S. (Edinburgh). Fourth edition, revised and enlarged. Price, $6.50. Pp. 350, with 245 illustrations and 3 colored plates. London: Henry Kimpton, 1942.

The third edition of "Traquair" was reviewed in the December 1938 issue of the ARCHIVES, page 1116. The present edition, which has 12 more pages of text and 18 more illustrations than its predecessor, is still the only monograph in English which deals adequately with the interpretation and evaluation of pathologic alterations of the visual fields as obtained by perimetry, and particularly by tangent screen scotometry.

In the first part of this volume 51 pages are devoted to the normal field of vision, perimetric and scotometric instruments and methods of examination. In the second part of the volume, after a comprehensive discussion of the pathologic field and an interpretation of the changes encountered, the author portrays, discusses and interprets the fields associated with glaucoma and lesions of the choroid, retina, optic nerve and chiasm in 152 pages. This portion of the volume should be of interest to all ophthalmologists. Twenty-nine pages are devoted to the suprachiasmal pathway, where most of the lesions and the resulting field defects are due to hemorrhage, thrombosis, tumor or injury. There are a short chapter on functional changes in the field of vision, an excellent appendix, a fairly complete bibliography, of 470 references, and author and subject indexes.

Traquair, whose work was developed from the principles of Bjerrum and Roenne, deserves acclaim because of his insistence on the use of weak stimuli (small visual angles) for detection of early changes in the visual fields. As he stated in a paper read before the American Ophthalmological Society (*Tr. Am. Ophth. Soc.* 37: 158, 1939), "A method which does not include he use of a visual angle of 2 minutes or less . . . cannot be regarded as adequate any more than a est card would be regarded as adequate which had no lines below 6/12." His apparatus for tangent screen scotometry is simple, inexpensive and effective. It consists of a tangent screen, which is used at a distance of 2 meters from the patient, a set of white and colored test objects from 1 to 60 mm. in diameter and 7 foot-candles of illumination. As Arnold Knapp has said: "It is not the elaboration of apparatus that is important but the understanding of the one who takes the field." One becomes increasingly aware of this because Traquair interprets and evaluates his fields in terms of the anatomic, physiologic and pathologic characteristics of that portion of the visuosensory system in which the lesion occurs which produces the pathologic field.

During the past twelve years I have had the opportunity of mapping tangent screen fields for almost every condition described by Traquair and have obtained fields of essentially the same types as he did. I agree entirely with his statements that relative yellow-blue blindness develops early in conditions affecting the outer layers of the retina and that "baring of the blindspot" is one of the earliest changes in the fields associated with glaucoma. Like him, I have been unable to find the so-called Seidel scotoma in cases of early glaucoma.

This is a book by a clinician for clinicians. Every resident in ophthalmology should be as conversant with its principles as he is with various surgical technics. Finally, it is indispensable for the ophthalmologist who believes that the examination of the fields, when indicated, is the most important part of the ophthalmologic work-up, and not something to be delegated to his office nurse or secretary.

WALTER F. DUGGAN.

Strabismus: Its Etiology and Treatment. By Dr. Oscar Wilkinson and Dr. Richard W. Wilkinson. Second Edition. Price, $4. Pp. 369, with 71 illustrations. Boston: Meador Publishing Company, 1943.

The first edition of this book was published in 1927. For those not familiar with the earlier edition, it should be said that it was written largely in digest form and was composed chiefly of quotations from other authors. This plan has been preserved in the present edition, and while the book contains a great deal of useful and interesting material, its disconnected form makes it difficult and unsatisfactory reading for the beginner. One of the outstanding features of the original volume was the review of the history of strabismus. It is with regret that one finds that many of the historical quotations have been cut and several interesting illustrations omitted. The same is true of the chapter on anatomy, in which the illustrations have been reduced to the point of inadequacy.

On the other hand, there are some important additions to the book. Under "Etiology," the section on heterophoria has been rewritten, with incorporation of the ideas of Duane. The operative treatment of paralytic strabismus has been enlarged, in keeping with approved present day teaching. Methods of diagnosis of anomalous retinal correspondence have been added; however, the authors seem to favor the expression "nonretinal correspondence," for which this re-

viewer can find little justification, as it will surely add to the general confusion.

The section on "Orthoptics" has been completely rewritten and enlarged, as it should be, to include the vast amount of work that has been done in this department in recent years. This section of the book is excellent, particularly in its discussion of occlusion and the use of the major amblyoscope.

The willingness of the authors to operate on a child at an early age, tempered with the proper caution, is most commendable. Their detailed, unbiased presentation of the chief operative procedures will be of interest to the experienced surgeon but will probably prove bewildering to the beginner. On the other hand, they give a definite answer to the question asked by every student of muscle surgery: "What and how much shall I do for a given deviation?" No doubt, the table giving exact operative procedures for different deviations is of value, in their hands, but it must be used with great caution by other surgeons. The authors have described several operations of their own that are worthy of careful study. Their use of a scale to measure the pull of an overactive muscle sounds like the answer to a long-felt want.

One finishes this book wishing that the authors had given more space to their own opinions and less to those of other workers.

MAYNARD WHEELER.

Blood Transfusion in Ophthalmology. Collective papers from the Ophthalmic Clinic of the Tashkent Medical Institute. Price, 3 rubles. Pp. 56. Tashkent, Uzbek Soviet Socialist Republic: State Publishers, 1941.

This book contains nine articles from the ophthalmic clinic of the Tashkent Medical Institute on the value of blood transfusions in the treatment of ophthalmic disease. Prof. P. F. Arkhangelsky and his associates have used blood transfusions since 1935. They employ mostly preserved blood (from one to sixteen days), in small quantities (from 75 to 250 cc.), with an interval of about ten days between transfusions. They regard the action of the blood as nonspecific, possibly accelerating the metabolism of the tissues and activating the reticuloendothelial system.

Blood transfusions were given in treatment of various diseases of the eyes, but the most striking results were obtained in cases of opacities of the vitreous, regardless of the cause and the next best in cases of hemorrhages in the retina and of soft lenticular matter in the anterior chamber after extracapsular extraction of the lens. Favorable results were also observed in cases of trachomatous pannus and keratitis associated with herpes zoster from the use of subconjunctival injections of blood (from 0.5 to 1.5 cc.). One of the authors (Meschersky) reported that 2 patients with chronic glaucoma responded well to blood transfusions, as the tension was lowered and the visual acuity and visual fields were increased. A few patients with blepharitis who did not respond to any type of therapy improved considerably with blood transfusion therapy. In some cases corneal transplants which had become opaque cleared up after the transfusion of blood. Transfusions, however, are not considered to be a panacea for all ills, and the authors state that the measure should be resorted to only when all others fail. Blood transfusion may also be employed as a prophylactic measure before intraocular operations. A plea is made for further study of the therapeutic action of the blood in pathologic conditions of the eye.

OLGA SITCHEVSKA

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu.

Chinese Ophthalmology Society

Presdient: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

Ophthalmological Society of the United Kingdom

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Place: Oxford, England. Time: July 8-9, 1943.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President: Dr. W. Belfort Mattos, Caixa Postal, 4086, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santa Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

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SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive. All correspondence should be addressed to the President.

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York City.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
Place: Chicago. Time: June 12-16, 1944.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. James A. Babbitt, 1912 Spruce St., Philadelphia.
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Executive Secretary-Treasurer: Dr. William L. Benedict, 101-1st Ave. Bldg., Rochester, Minn.

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Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.
Place: Hot Springs, Va. Time: May 29-31, 1944.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
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CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

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Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. R. Evatt Mathers, 34½ Morris St., Halifax, N. S.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.
Place: Halifax, N. S. Time: Aug. 4-5, 1944.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

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Secretary: Dr. G. L. McCormick, 626 S. Central Ave. Marshfield.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Paul A. Chandler, 5 Bay State Rd. Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. L. L. McCoy, 1317 Marion St., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. H. Pike, Midland, Mich.
Secretary-Treasurer: Dr. R. H. Criswell, 407 Phoenix Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

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Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

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Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
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SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Ray Parker, 218 Franklin St., Johnston. Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

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Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. C. A. Ringle, 912–9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
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INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Val H. Fuchs, 200 Carondelet St., New Orleans.
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MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

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MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings, Mont.
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New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr B. E. Failing, 31 Lincoln Park, Newark.
Secretary: Dr. George Meyer, 410 Haddon Ave., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. James E. McAskill, 508 Woolworth Bldg., Watertown.
Secretary: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. T. W. Buckingham, 405 Broadway, Bismarck.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St, Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St, San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave, Dallas.

Utah Ophthalmological Society

President: Dr. R. B. Maw, 699 E. South Temple, Salt Lake City.
Secretary-Treasurer: Dr. Charles Ruggeri Jr., 112 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave, Fairmont.
Secretary: Dr. Welch England, 621½ Market St, Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. E. L. Mather, 39 S. Main St., Akron Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. William B. Agan, 1 Nevins St., Brooklyn.
Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. Walter F. King, 519 Delaware Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman: Dr. Shandor Monson, 1621 Euclid Ave., Cleveland.
Secretary: Dr. Carl Ellenberger, 14805 Detroit Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Alfred Cowan, 1930 Chestnut St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. H. D. Emswiler, 370 E. Town St., Columbus, Ohio.
Secretary-Treasurer: Dr. D. G. Sanor, 206 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Arthur Padillo, 414 Medical Professional Bldg., Corpus Christi, Texas.
Secretary: Dr. Edgar G. Mathis, 815 Medical Arts Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Abell Hardin, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

DETROIT OPHTHALMOLOGICAL CLUB

Chairman: Dr. Howell L. Begle, 2730 E. Jefferson Ave., Detroit.
Secretary: Dr. C. W. Lepard, 1025 David Whitney Bldg., Detroit.
Time: 6:30 p. m., first Wednesday of each month, November through April.

DETROIT OPHTHALMOLOGICAL SOCIETY

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President: Appointed at each meeting.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

EASTERN PENNSYLVANIA ASSOCIATION OF EYE, EAR, NOSE AND THROAT PHYSICIANS

President: Dr. James E. Landis, 232 N. 6th St., Reading.
Secretary-Treasurer pro tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.
Time: Last week in April each year.

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SECTION

President: Dr. Felician J. Slataper, 1110-1111 Medical Arts Bldg., Houston, Texas.

Secretary: Dr. Theo. L. Holland, 611 Medical Arts Bldg., Houston, Texas.

Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

INDIANAPOLIS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.

Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.

Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.

Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.

Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.

Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.

Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. E. Trainor, 523 W. 6th St., Los Angeles.

Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

LOUISVILLE EYE AND EAR SOCIETY

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time. 6:30 p. m., second Thursday of each month from September to May, inclusive.

LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Each member in alphabetical order.

Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Each member in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. Edwin C. Bach, 324 E. Wisconsin Ave., Milwaukee.

Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.

Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.

Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.

Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

MONTREAL OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.

Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.

Time: Second Thursday of October, December, February and April.

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.

Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashvile, Tenn.

Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.

Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

NEW ORLEANS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.

Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.

Place: Louisiana State University Medical Bldg Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Frank C. Keil, 660 Madison Ave., New York.

Secretary: Dr. Willis S. Knighton, 121 E. 61st St., New York.

Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Sigmund Agatston, 875–5th Ave., New York.

Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.

Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.

Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.

Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. D. D. Stonecypher, Nebraska City, Neb.

Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.

Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.

Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.

Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.

Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.

Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. John B. McMurray, 6 S. Main St., Washington, Pa.

Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.

Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. R. M. Brickbauer, Shillington, Pa.

Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading Pa.

Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.

Secretary: Dr. Clifford A. Folkes, Professional Bldg. Richmond, Va.

Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St. Rochester, N. Y.

Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. C. C. Beisbarth, 3720 Washington Blvd. St. Louis.

Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd., St. Louis.

Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.

Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.

Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.

Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.

Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.

Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.

Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Felician J. Slataper, 1110-1111 Medical Arts Bldg., Houston, Texas.

Secretary: Dr. Theo. L. Holland, 611 Medical Arts Bldg., Houston, Texas.

Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.

Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.

Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.

Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.

Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.

Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.

Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. M. E. Trainor, 523 W. 6th St., Los Angeles.

Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time. 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.

Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Edwin C. Bach, 324 E. Wisconsin Ave., Milwaukee.

Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.

Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.

Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.

Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.

Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.

Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.

Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashvile, Tenn.

Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.

Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Oto-laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.

Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.

Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Frank C. Keil, 660 Madison Ave., New York.

Secretary: Dr. Willis S. Knighton, 121 E. 61st St., New York.

Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. Sigmund Agatston, 875–5th Ave., New York.

Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.

Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.

Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.

Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. D. D. Stonecypher, Nebraska City, Neb.

Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.

Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p.m. dinner; 7 p.m. program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.

Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.

Place: Paterson Eye and Ear Infirmary. Time: 9 p.m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.

Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.

Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. John B. McMurray, 6 S. Main St., Washington, Pa.

Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.

Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

READING EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. R. M. Brickbauer, Shillington, Pa.

Secretary: Dr. Paul C. Craig, 232 N. 5th St., Readin Pa.

Place: Wyomissing Club. Time: 6:30 p. m., thi Wednesday of each month from October to July.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Peter N. Pastore, Medical College Virginia, Richmond, Va.

Secretary: Dr. Clifford A. Folkes, Professional Bld Richmond, Va.

Place: Westmoreland Club. Time: 6 p. m., seco Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Frank Barber, 75 S. Fitzhugh S Rochester, N. Y.

Secretary-Treasurer: Dr. Charles T. Sullivan, 2 Alexander St., Rochester, N. Y.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. C. C. Beisbarth, 3720 Washington Blv St. Louis.

Secretary: Dr. H. R. Hildreth, 508 N. Grand Blv St. Louis.

Place: Oscar Johnson Institute. Time: Clinical mee ing, 5:30 p. m., dinner and scientific meeting 6: p. m., fourth Friday of each month from October April, inclusive, except December.

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Belvin Pritchett, 705 E. Houston St San Antonio 5, Texas.

Secretary-Treasurer: Lt. Col. John L. Matthews, AA School of Aviation Medicine, Randolph Field, Texa

Place: San Antonio, Brooke General Hospital, Ra dolph Field or San Antonio Aviation Cadet Cente Time: 7 p. m., second Tuesday of each month fro October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Roy H. Parkinson, 870 Market St San Francisco.

Secretary: Dr. A. G. Rawlins, 384 Post St., Sa Francisco.

Place: Society's Bldg., 2180 Washington St., San Fran cisco. Time: Fourth Tuesday of every month excep June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg Shreveport, La.

Secretary-Treasurer: Dr. Kenneth Jones, Medical Art Bldg., Shreveport, La.

Place: Shreveport Charity Hospital. Time: 7:30 p.m first Monday of every month except July, Augus and September.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Felician J. Slataper, 1110-1111 Medical Arts Bldg., Houston, Texas.

Secretary: Dr. Theo. L. Holland, 611 Medical Arts Bldg., Houston, Texas.

Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-Laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.

Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.

Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.

Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.

Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.

Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.

Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. M. E. Trainor, 523 W. 6th St., Los Angeles.

Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time. 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.

Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Edwin C. Bach, 324 E. Wisconsin Ave., Milwaukee.

Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.

Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.

Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.

Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.

Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.

Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.

Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashvile, Tenn.

Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.

Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Oto-Laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.

Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.

Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Frank C. Keil, 660 Madison Ave., New York.

Secretary: Dr. Willis S. Knighton, 121 E. 61st St., New York.

Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. Sigmund Agatston, 875–5th Ave., New York.

Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.

Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.

Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.

Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. D. D. Stonecypher, Nebraska City, Neb.

Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.

Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p.m. dinner; 7 p.m. program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.

Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.

Place: Paterson Eye and Ear Infirmary. Time: 9 p.m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.

Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.

Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. John B. McMurray, 6 S. Main St., Washington, Pa.

Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.

Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

READING EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. R. M. Brickbauer, Shillington, Pa.

Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.

Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.

Secretary: Dr. Clifford A. Folkes, Professional Bldg. Richmond, Va.

Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Frank Barber, 75 S. Fitzhugh St. Rochester, N. Y.

Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. C. C. Beisbarth, 3720 Washington Blvd. St. Louis.

Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd. St. Louis.

Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.

Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.

Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.

Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.

Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.

Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.

Place: Shreveport Charity Hospital. Time: 7:30 p.m., first Monday of every month except July, August and September.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.

Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.

Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.

Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.

Place: University Club. Time: First Tuesday of each month except June, July and August.

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. E. A. Orwig, 420 Madison Ave., Toledo, Ohio.

Secretary: Dr. E. W. Campbell, 316 Michigan St., Toledo, Ohio.

Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.

Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.

Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. S. Bockoven, 1752 Massachusetts Ave., Washington, D. C.

Secretary-Treasurer: Dr. John Lloyd, 1218-16th St. N. W., Washington, D. C.

Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.

Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.

Place: Office of chairman. Time: Last Tuesday of each month from October to May.

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TRAUMATIC LIPORRHAGIA RETINALIS (VERHOEFF*)

PURTSCHER'S DISEASE

EDMUND B. SPAETH, M.D.

PHILADELPHIA

Many interesting papers have been written on this condition since the first article, published by Donders in 1871. Stokes, in 1932, Malbrán, in 1940 and Smith, in 1941, have covered the literature rather well, though several other important contributions should be included in a complete bibliography of this condition. In this paper an attempt has been made to list important references which have appeared to date in the various ophthalmologic journals, so that they may be available for use in any further investigations.

My purpose in this somewhat detailed search was to obtain, if possible, a more satisfactory explanation of the pathologic changes in the eye and to determine the mechanical basis of the retinal hemorrhages, the reasons for the many different types of hemorrhages, the cause of the extensive perivasculitis observed in several cases and, finally, the cause of the exudative processes so commonly seen in the macula, as well as in other portions of the retina. The causes proposed varied from possible rupture of the thoracic duct, with resulting lymphorrhagia (never proved clinically) to the direct effect of hemorrhages, and from albuminuria, as a sign of a pure inflammatory process, to an abrupt increase in intracranial pressure, with resultant vascular changes in the retina, these changes being transmitted through the perivascular lymph spaces. In fact, even the possibility of the cerebrospinal fluid's being forced into the retina proper by the pressure exerted through the perineural-perivaginal lymph spaces has been proposed by Purtscher. This hypothesis is based on Leber's observations and conclusion that "the intervaginal space of the optic nerve passes directly into the subarachnoid space and thence directly into the cerebral ventricle, so that the possibility of entrance of cerebrospinal fluid through the intervaginal space must be conceded."

According to Albert and Schnitzler, in cases of artificially increased cerebral (intracranial) pressure there is a continuous flow of cerebrospinal fluid from the optic nerve sheath, whereas normally the fluid escapes only in drops. Hence Leber stated:

> . . . Though the intervaginal space usually ends blindly, anteriorly, experiments with injections have demonstrated connections of this space with the supravaginal space and with Tenon's space, and even with the perichoroidal space, and through that, via the lymph sheaths, with the central vessels of the optic nerve.

There exists of course the further possibility that under certain circumstances the cerebrospinal fluid actually enters the aforementioned spaces, where it may produce changes.

> [If] however, this occurs via the lymph sheaths of the central vessels of the optic nerves, i. e., as a result of excess pressure in the former, it is logical to conclude that under high pressure the stasis of lymph in the perivascular spaces of the central vessels will result in passage of the lymph along the continuation of the spaces about the ramifications of the retinal vessels into the retina, where it may also produce changes (Leber).

While this transmission of the lymph may be a causal factor in some instances, the theory does not answer adequately all the questions. In certain of Purtscher's original cases the condition was associated with trauma to the head, and not to the trunk, and thus the mechanical agent might well have been different.

From the Wills Hospital.

This paper, with a report of the 2 cases, was presented at a meeting of the College of Physicians of Philadelphia, Section on Ophthalmology, Nov. 17, 1942. An abstract of the paper, with discussion, appeared in the April 1943 issue of the ARCHIVES, page 696.

* Prior to the submission of this paper for publication, and after its presentation before the Section on Ophthalmology, College of Physicians of Philadelphia, the manuscript was sent to Dr. F. H. Verhoeff for comments. His suggestions were of tremendous value. A comment of outstanding importance follows:

"In short, I conclude that two factors are necessary to produce the condition, namely, considerable obstruction to venous outflow and hyperlipemia, and that the white spots are due not to embolism but to extravasation of fat into the retina. As a name for the condition I suggest traumatic liporrhagia retinalis." Other suggestions of Dr. Verhoeff's appear in relevant positions in this paper. It is of further interest and significance that Verhoeff wrote of the condition as Purtscher's retinosis, a fact easily overlooked. This qualifying term answers rather definitely some of the queries in the earlier literature.

If grave degrees of change in the cavernous sinus, as well as other cerebral venous sinuses, were responsible for the ocular signs, then one should later observe, at least occasionally, papilledema and oculomotor disturbances from the continued intracranial pressure which would follow thrombosis of these sinuses. Papilledema would certainly develop in cases of less severe damage, without loss of life, even though the fundic picture of Purtscher's disease might be present clinically.

Recent studies of the development of papilledema and experimental and clinical examinations all have shown that the effects of intracranial pressure through passage of the cerebrospinal fluid along the vaginal spaces of the nerve are so slow in development, even with space-taking lesions of considerable size, that Purtscher's hypothesis is hardly tenable. Further, the slow recession (in the ophthalmic picture) of papilledema after the release of all abnormally high intracranial pressure differs definitely from the rapid recession in cases of angiopathia retinae traumatica. The basic premise in Purtscher's hypothesis, however, does not differ from that which I feel is significant in the development of papilledema. Another point is the almost constant absence of any state of mental retardation or mental confusion in cases of Purtscher's disease

Purtscher's hypothesis, with respect to the mechanism involved, is not sustained by the evidence in the first of the 2 cases to be presented here. In this case the condition was not Purtscher's disease, but simply pronounced congestion of the retinal veins and arteries, due to compression of the chest with associated fractures. Hence the case indicates a possible relation between the intracranial venous sinuses and disturbances in the retinal circulation. In view of this possibility, an indefinite secondary effect may be exerted on the development of Purtscher's disease through the intracranial venous circulation. It is sufficient to know to a certainty that severe injuries to the trunk and abdomen (demonstrated clinically, as well as by various accepted animal experiments) may cause thrombosis of one of the cranial venous sinuses, as the most extreme degree of damage possible.

Verhoeff stated:

> The white spots characteristic of Purtscher's retinosis never occur in ordinary cases of increased intracranial pressure, even when this is extremely high. They also never appear after thrombosis of the cavernous sinus or complete obstruction of the central vein. Hence, they must have some other cause. They occur only in cases in which there have been fracture and obstruction of the retinal veins. Their appearance strongly suggests the presence of fat. Simple obstruction or embolism of a retinal vessel never produces them; therefore emboli would not do so. Most likely they are due venous obstruction associated with traumatic hyp lipemia. Distention of the small vessels might p the fat to pass into the tissues, either by diapedesis through small breaks in the distended vessels. Usual some blood is extravasated with the fat.

It is interesting that so few persons have con sidered the possibility that fat emboli (fat dro lets) arising from traumatized bone marrow from damaged bone substance are sufficient t explain the retinal changes. In view of this po sibility the presence of the fundic picture char acteristic of septic endocarditis certainly the serious consideration of that condition as probability in all instances in which there h been injury by compression to bone. It is fair well known that emboli from injured bone row may produce multiple infarcts in dis organs and structures.

Oppolzer, in 1933, studied exhaustively the occurrence of fat emboli following multiple fr tures and severe contusions of the subcutane fatty tissue. Experimentally, Czerny and Bill roth, in 1875, demonstrated hemorrhages in choroid in dogs following injections of hog into the jugular vein. In spite of this, stated "that no case has been observed in whi demonstrable visual disturbance developed as result of fat embolism." Oppolzer apparent took this statement of Leber's as his gage of con troversy in proving his contention. He first fully analyzed the literature and cited repeat instances in which the clinical observation h been made. For instance, Wilke reported presence of hemorrhages in the choroid of dog with fat embolism following transverse fr tures of both hindlegs. Busch and Wilke re ported fat globules in the capillaries of the con junctiva. Hosch, as early as 1905, examined the retina, as a surface specimen, of a man who had died with fat embolism of the lung fifty-fo hours after an accident and observed fat in the retinal capillaries. Schieck learned (through personal communication) that his colleag Bunge, of Halle, Germany, had concluded fr his rich experience that "after mine acciden white foci can almost constantly be demonstrated in the retina." Schieck classified these changes with the retinal lesions described by Purtscher (1910), without, however, drawing attention to the possible etiologic significance of fat droplets.

Oppolzer made a detailed clinical and histo pathologic examination of 7 cases of tra in which fat emboli could have occurred becau of the nature of the trauma. In addition, he re ported a possible case of Purtscher's disease, in which the patient had a craniotomy after exten sive injuries sustained in a fall of four stories

Autopsy revealed fractures of the pelvis, the vertebrae, both ankles, the upper portion of the arm and the base of the skull. The results of examination of the tissues were reported. An abstract of this study follows:

Fat embolism in the greater circulation often leads to changes in the eyegrounds, which can be demonstrated by more frequent examinations, even after days and weeks. These changes are also demonstrable in cases of severe cerebral or pulmonary fat embolism but are more frequent in cases of the cerebral form. They can be demonstrated ophthalmoscopically as emboli in the direct branches of the central artery. Histologically the white foci are characterized by edema of the nerve fiber layer of the retina overlying capillaries with fat emboli, a change which is also demonstrable in both brain and nerve substance. These retinal changes usually do not cause disturbance of vision, but if located in the macula they may lead to severe and lasting visual loss In the presence of obscure cerebral symptoms due to injury, such a fundic picture may be of diagnostic significance. As a rule these lesions heal, leaving no trace.

Secondary retinal changes occurred in 6 cases of fat embolism, with histologic changes and clinical symptoms characteristic of cerebral fat embolism. In 4 of these cases of severe cerebral fat embolism the patient recovered.

Pronounced vascular changes in the brain were observed in 1 case of cerebral fat embolism, and then only in the globus pallidus.

The retinal changes associated with fat embolism showed a possible relation to late post-traumatic injuries of the retina.

The cerebral cortex itself did not show any characteristic severe changes. The cells were well preserved, and the glia was not reddened or proliferated. There were no softenings or hemorrhages. In the medullary layer of the cerebral cortex the changes were more pronounced. Especially in the medulla of the frontal portion of the brain and of the capsule one could observe the following changes: There were numerous hemorrhages from vessels of various calibers. In other cases and in other places in the same eyes the bleeding came from the capillaries. If the hemorrhage was severe, the wall of the bleeding vessel frequently could no longer be recognized. Elsewhere the walls could be identified as strips of tissues permeated with blood or as coagulated tissue rests in the center of the hemorrhages. Occasionally there appeared a tiny extravasation of blood from the vessels, the walls of which showed lesions.

Besides these two forms of hemorrhage, there was in the internal capsule, at the margin of the striatum, a small white softening. An area of meshlike structure could be recognized, in which the tissue was destroyed.

A common observation in all the areas examined was the filling of numerous blood vessels with fat. Both in the cortex and in the white substance of the cerebrum, the striatum pallidum, the optic thalamus, the medulla oblongata and other portions of the brain stem the lumens of some of the vessels were more or less abundantly filled with fat. However, the presence of fat in the vessels did not produce a secondary reaction of nerve tissue, or even of the vessel walls.

In the discussion on the first presentation of the cases to be reported here, Shipman stated that he was not well satisfied with the theory that fat emboli (fat droplets) were the cause of the lesions. It seemed to him that if fat embolism was the etiologic factor, the condition should be encountered more commonly. This opinion is not surprising; in fact, it is rather common. Winkelman called attention to this controversy. For instance, Gröndahl, cited by Winkelman, could not prevent fat embolism even after ligation of both the venous and the lymphatic drainage of the extremities of experimental animals. Lehman, also cited by Winkelman, maintained that fracture could not disorganize all the fat cells in the bone marrow and that it was impossible to explain the forcing of fat into the veins, for while the course of the venous current above an injury is away from the site of the lesion, the pressure in the vein is positive, not negative. Lehman stated that veins never exert suction and that as all currents lead toward, and not away from, the site of injury, fat can hardly enter damaged veins.

The course which the fat droplets may take after they enter the circulation is more certain than its origin or its method of entrance. To postulate an open foramen ovale is unnecessary, though 1 case (Fuchsig) of pulmonary fat embolism was reported in which there was an open foramen ovale. On the other hand, cases have been reported in which free fat droplets were present in the urine after trauma, the lungs themselves being free. Under such circumstances the systemic circulation must have conveyed the fat emboli. Therefore the fat droplets had to pass through the pulmonary circulation, in spite of this having been called "the guardian angel of the systemic circulation."

It is a fact well known to the general surgeon that small fat globules acting as emboli are not infrequently the complication of a broken bone, usually of an extremity. These globules pass through the pulmonary veins and the left side of the heart, ultimately to lodge in the brain. The brain may show no gross lesions other than multiple petechial hemorrhages due to the emboli scattered throughout the centrum. It is not at all uncommon for death to occur from cerebral fat embolism within a few days, while in other cases the course goes on to ultimate recovery. The pathways to the terminal retinal vessels, while appreciably shorter, are much more devious than those to any part of the cerebral cortex. This may be the answer to the relative infrequency of retinal angiopathy as compared with the more common occurrence of cerebral fat embolism.

It is true, as Shipman pointed out, that Knoll and Willers independently trephined the skulls

of rabbits and found that the brain could be made to bulge through the trephine holes when pressure was applied to the thorax or to the abdomen. Nevertheless, an increase in intracranial pressure, no matter how sudden or how extensive, cannot account for the characteristic exudates in the retina seen at various times. These exudative areas vary from massive white, milky swellings to white plaques (figure) and many discrete, elevated areas, resembling cotton wool, which lie along the vessels. These areas show striae and many hemorrhages contiguous to the vessels and apparently are not connected with or related to the white spots. The presence of fat droplets apparently could account wholly for the changes. Certainly, petechial hemorrhages constitute a classic characteristic of emboli.

Purtscher's original description is not clearcut. Salient points in some of his cases are noted here in translation (the italics, which are mine, indicate characteristics in common between Purtscher's original description and the picture in the second of the 2 cases presented here).

The ophthalmoscopic picture in such cases is characterized by white spots, usually located in the innermost layers of the retina and showing a close relation to the course of the retinal veins. For this reason they appear predominantly in the region about and on the disk and the *macula lutea.*

In the great majority of cases there appear numerous striate and punctate hemorrhages.

Symptoms of papillitis may complete the picture but may be absent.

The predominant feature is *bright, dazzling white specks* and effusions of blood. The disks may be entirely normal, sharply defined and nonhyperemic, the vessels being of normal caliber and the arteries perhaps a bit more tortuous than normal, but hardly pathologic.

The changes to be described in detail involved predominantly the region *between the disk and the macula* but, following the course of the vessels, extended 3.6 disk diameters toward the periphery of the retina. It was immediately evident that the changes closely followed the veins; *the arteries appeared not to be involved.*

In 1 case ophthalmoscopic examination of the right eye revealed a large so-called preretinal hemorrhage, 2 disk diameters in extent, of a shagreen appearance. It sprang from the superior temporal vein, which bounded the hemorrhage above. Also, in the region of the inferior retinal veins, for instance around the inferior temporal vein, fairly extensive, thin venous hemorrhages, produced by diapedesis, appeared in the retina; these in part showed fine vertical striations.

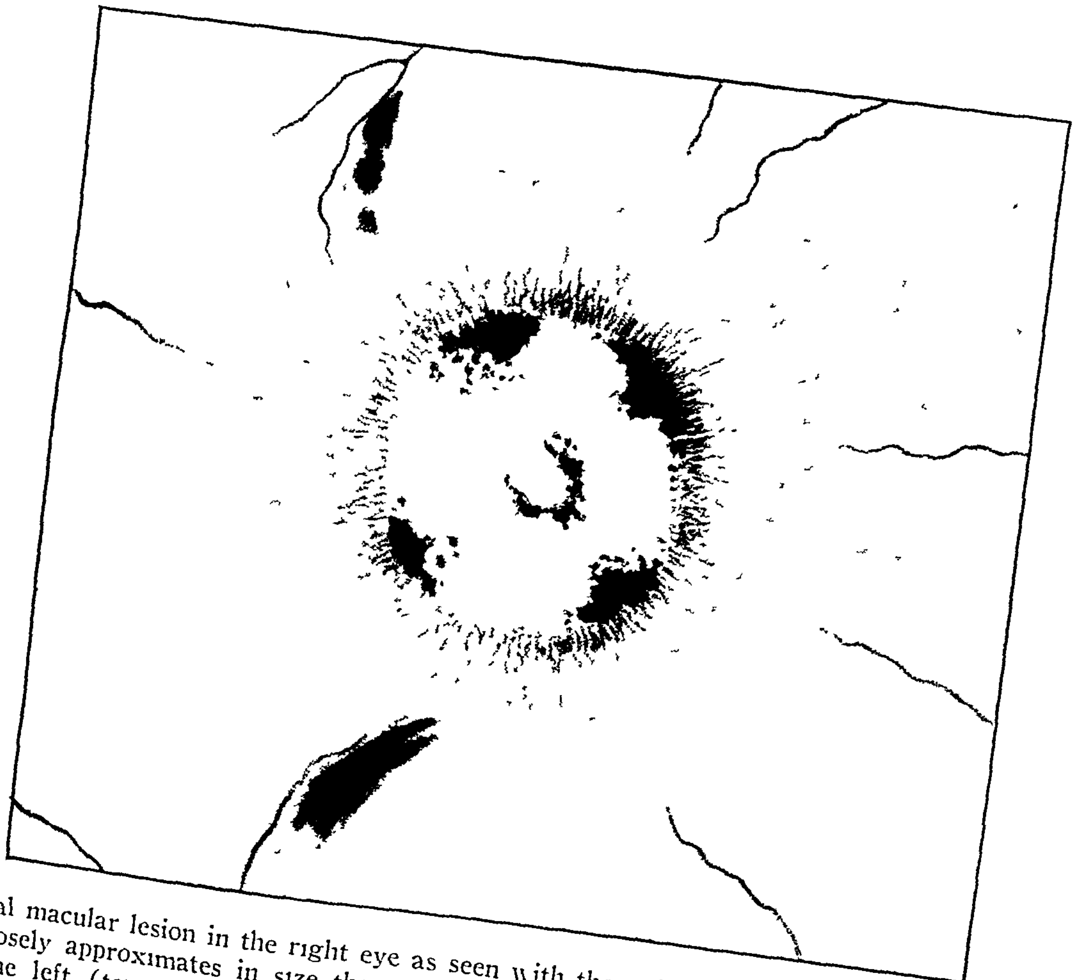
The most interesting observation in another case was the presence of twenty-nine white specks in the fundus, of various sizes and shapes. Their long diameters (which paralleled the vessels) ranged from 0.2 to 1 disk diameter; the breadth varied. Usually they were approximately oval, but some were elongated. *Frequently they obscured the veins, to which they showed an intimate relation,* and could thus be located in the innermost layers of the retina. The appearance and outlines of the specks suggested scattered snowflakes. Their margins *were indistinct, splitting into very fine striae and punctae, which could be more plainly d[is]tinguished in individual plaques.* In color they w[ere] bright silver, with a rather bluish tinge. The sp[ecks] seemed to have a certain predilection for the [small] venous branches springing from the macula and [their] ramifications, so that the latter appeared between [the] white specks somewhat as rivers on a map betw[een] elevations of the terrain. These small vessels—possi[bly] by contrast—showed up sharply and were prob[ably] fuller than normal. Similar peculiar changes, exc[ept] for the large hemorrhage, were observed in the fu[ndus] of the left eye, but here the hemorrhages were alm[ost] entirely absent. Only a few hemorrhages of sl[ight] degree were noted along the inferior temporal vein, a[nd] two insignificant, round hemorrhages were seen abo[ve] between two white spots. The centers of both [maculae] showed unusually coarse, indistinct, brownish stipp[ling]. No foveal reflex could be seen.

The white specks showed unmistakable rapid ret[ro]gression, diminishing in extent and density and d[is]solving more and more into fine, silvery bright p[oints] and striae.

My 2 cases are now presented, the first in ab[]stract and the second in detail.

Case 1.—A man aged 40 was admitted to the [hos]pi[tal] several hours after he had sustained a severe cr[us]hi[ng] injury to the chest as the result of his being s[queezed] between the back of a large truck and the side of a sto[ne] building. The patient died several hours after a[dmis]sion. The bony thorax had many simple and [compound] fractures. A few hours prior to his death [examination] of the fundus showed a picture which resembled, to [a] remarkable degree, that seen in cases of poly[cythemia] vera. There were tremendous engorgement and tor[tu]osity of all the retinal veins and arteries, with man[y] massive retinal hemorrhages. The onset of the r[etinal] angiopathy was apparently almost instantaneous. T[he] patient was mentally clear and did not present th[e] common picture of severe cranial trauma.

Case 2.—A streetcar motorman on Oct. 29, 1942 w[as] forcibly thrown against the front of his car in [a] collision, when the car which he was driving [] derailed after going through an open switch. He complained immediately of pain in his chest and, *with[in] an hour,* of impaired vision. The patient was sent [to] the Municipal Hospital and from there to his company's infirmary. Roentgenograms of the chest [were] taken without delay and apparently showed noth[ing] abnormal. No definite symptoms of injury to the che[st] were present except for the pain. The police examinations thought necessary prevented further medical examination until the following day. The patient was mentally alert and clear throughout all these investigations, showing no sign of cranial trauma. Examination revealed no pathologic external changes in the eyes. The pupillary reflexes were normal, and oculomotor motility was normal. Vision, with the best correction, was 6/12 in each eye, being slightly better in the left eye than the right. Examination of the fundi showed venous tortuosities; edema, with massive "exudates" into each macula; rather extensive perimacular edema and infiltration, with radiating tension lines about the right macula; many fine hemorrhages into each macula, and grosser extramacular hemorrhages, which tended to be flame shaped. The hemorrhages were largely venous and, with the exception of those in the macula in close proximity to a vein, usually involved the smaller veins; two of the arteries, however, also showed hemorrhages, as seen in the figure. This drawing presents the lesion



Central macular lesion in the right eye as seen with the red-free light. The central macular plaque closely approximates in size the normal papilla. The flame-shaped hemorrhage below, toward the left (temporal) margin, is in proximity to an arteriole, while that above, on a branched vessel, is near a venule. The corona of droplet hemorrhages about the central lesion is pictured perhaps as a bit more extensive (though only slightly so) than the actual lesion. The yellowish tint of the central portion of the plaque was best seen with green illumination—in fact, it was barely visible with ordinary light. Vision in the right eye was 6/12 at the height of the pathologic process

in the macula of the right eye as seen with red-free light, the lesion being the size of the normal papilla. A macular lesion in the left eye was similar, though less extensive. There were five smaller white spots scattered about, all in close proximity to the terminal vessels; at least one of these patches lay on a terminal arteriole, overlying and in fact almost ensheathing, the vessel. The last-mentioned lesion was in the inferior temporal extramacular region. It was yellowish white, and rather sharply demarcated, but was not hemorrhagic. Another, smaller lesion, irregularly triangular, lay between the parallel courses of the superior temporal artery and its vein (left eye), its margins being rather indistinct and directed toward the papilla, though its peripheral outlines were in part rather distinct. In the apex of this lesion were a few tiny droplet hemorrhages, within and just outside its edges. This indistinct outline corresponded exactly with Purtscher's, the original description. Its relation was apparently anatomic and followed the course of the retinal nerve fibers.

The largest retinal area, that is, the macula, was silvery as viewed with red-free light (figure) and yellowish with ordinary ophthalmoscopic light. It was outlined with very fine lines of droplet hemorrhages arranged like a corona, and the elevated plaque had denser hemorrhages. In addition, there was a ring of hemorrhages in the center; this central portion, which is supplied by the choroidal circulation, appeared yellow. It may be significant that this yellow area was the last to disappear during the process of absorption. This large plaque lay deep in the retinal stroma, a fact even more evident a bit later, when, during the days of rapid absorption, the yellowish tint of the central region faded slowly, remaining even after the brown stippling of the absorbing hemorrhages had wholly disappeared. The retina about the macula was edematous, with fine radial striations which were faint but were rather easily seen, especially when the illuminated area was viewed somewhat obliquely.

According to this description of the lesions observed, both venous and arterial structures may be involved. This fact is significant. Purtscher himself stated that the characteristic of the disease is "the appearance of white plaques in retinal areas in otherwise apparently normal condition, and quite independent minimal hemorrhages in other parts of the retina, their independence indicating their separate origin."

The peripheral fields were normal. The central fields showed changing and rapidly receding central scotomas.

The patient was admitted to the hospital and was carefully studied for any possible clinical signs which might suggest the mechanical basis of the retinal changes. None whatever was found. All of the studies gave wholly normal or negative results. The internist called in on the case expressed the opinion that the patient had costal-sternal compression and trauma (dislocations) in view of the persistent pain in the thorax over these regions. Strapping of the chest and diathermy treatments, when started, gave him relief in ten days to two weeks. It was thought that the patient might have had a preexisting cardiovascular-renal condition, but detailed study revealed nothing abnormal. His blood pressure averaged 140 systolic and 90 diastolic.

Fourteen days after the accident the patient's vision had cleared to 6/6 — 2 and was 6/5 — 2 with the best correction. The fundus of the left eye was normal except for a possible slight arteriovenous disproportion. The fundus of the right eye was also normal except for slight depigmentation of the macula and for the remains of the yellow tint in the central portion of the macular hemorrhage.

Eight months later the patient had tiny bilateral absolute central scotomas without any visible changes in the fundus, and visual acuity was 6/12 and 6/9. This condition is apparently permanent. In some of the cases reported in the literature varying degrees of optic nerve atrophy resulted. In these cases the initial injury was probably more severe than in our case 2.

COMMENT

In the first of the 2 cases presented here notable vascular changes appeared in the retina immediately after the injury. The patient died shortly thereafter. There should be considered, first, the probability, in case Purtscher's disease was to develop, that death occurred before the exudates could develop about the terminal vessels containing fat droplets and emboli. The tremendous engorgement of the veins, especially those with the multiple massive hemorrhages, suggests a second possibility, that is, thrombosis of the intracranial venous sinuses and the resulting abrupt stasis in the retinal veins.

Purtscher, in his original paper, emphasized the relation of the exudates and hemorrhages to the veins. In the second case reported here, the pathologic process was associated with at least two arterioles. Further, at least one pathologic patch was of truly capillary origin and was equally close to an artery and to a vein. In the terminal circulation of the eye it seems necessary to associate emboli with the arterioles rather than with the venules. Purtscher's hypothesis is based on perivascular changes associated with venules. If fat droplets present as emboli are to be considered of etiologic importance, then both capillary and arteriolar changes and relations should be observed. Such observations were made in the second case.

CONCLUSIONS

On the basis of a study of the 2 cases presented and a critical review of the literature, the following conclusions are relevant:

1. The term retinal teletraumatism, suggested by Smith, is not sufficiently descriptive, and hence is unsatisfactory. The original term angiopathia retinae traumatica is equally inapt in that it fails to eliminate such cases as the first one reported here. Furthermore, and more important, the term fails to take into account the basic etiologic and pathologic factors. Verhoeff's suggestion, "traumatic liporrhagia retinalis," seems adequate. The term designates the exact etiologic agent, the anatomic structure involved and the precipitating cause.

2. The reasons for the various retinal changes seen and reported are not, as Stokes said "only speculative."

3. Several allied conditions, such as traumatic asphyxia, have similar lesions, and such lesions might be the result of an etiologic factor somewhat similar to that present in the first case reported, i.e., involvement of the intracranial venous sinuses.

4. The onset of angiopathy is abrupt and occurs early in the course of the disease. Arterioles may be involved, in spite of Purtscher's original statement. This presupposes that the minute fat emboli, i.e., fat droplets, have passed through the pulmonary circulation. This must occur for the condition cannot be the result of pathologic changes in the venules alone, as originally postulated by Purtscher. The fact that venules also show changes seems to indicate that the fat droplets have entered. and even passed through, the capillaries. Verhoeff stated (personal communication):

> It would seem that minute fat globules could pass through the wall as readily as red blood corpuscles, if not more so. The complete recovery of retinal function and the rapid absorption of the fat indicate that there has been no obstruction in the affected vessels—even temporary complete obstruction would permanently destroy retinal function in the region supplied by the vessels.

This statement is significant in consideration of the mechanics of the condition and the exact whereabouts (anatomically) of the fat droplets, as these are represented by the visually evident white spots and the varied hemorrhages.

5. It is certain that the condition in these cases is not purely the result of thrombosis of the intracranial vascular sinuses or of a sudden increase of intracranial pressure sufficient to account for the retinal changes seen and postulated by Purtscher on the basis of the cerebrospinal fluid's being forced along the vaginal sheath. The first of these two factors has a possible relation; the importance of the second is denied. It is almost certain that fat emboli as droplets are responsible for the majority of cases of angiopathia retinae traumatica (traumatic liporrhagia retinalis), modified in part perhaps by thrombosis of cerebral venous sinuses. It is doubtful whether an increase in intracranial pressure is present in these cases. Certainly, it is not a necessary or important, or even a significant. etiologic factor. The complete absence of any mental signs or other symptoms of increased intracranial pressure in all the cases reviewed is important.

6. Liporrhagia retinalis traumatica is characterized by a somewhat generalized diffusion of fat droplets in the fundus, the picture being modified in part by a generalized hemorrhagic situation in the retina or brain or both due to factors other than the emboli themselves, that is, probably severe disturbance in the venous circulation of the retina, brain and brain stem.

1930 Chestnut Street.

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PATHOLOGIC CHANGES IN THE EYE ASSOCIATED WITH SUBACUTE BACTERIAL ENDOCARDITIS

REPORT OF FIVE CASES WITH AUTOPSY

EVA C. DIENST, M.D., AND SAMUEL GARTNER, M.D.
NEW YORK

Subacute bacterial endocarditis is a complication of heart disease which is often brought to the attention of the ophthalmologist because of the striking fundic picture. We had the opportunity of obtaining at autopsy the eyes of 5 patients who died of this disease at Montefiore Hospital. The ocular lesions were of special interest, as they were visible to a considerable extent during life and often suggested the diagnosis early. Christian [1] stated that only early diagnosis offers any hope of aid from chemotherapy.

According to Libman and Friedberg [2] the disease is due to infection with bacteria of low virulence of an abnormal heart. The abnormality may be congenital malformation, such as patency of the interventricular septum, pulmonary stenosis or patency of the ductus arteriosus, but is usually the result of chronic valvular disease of the rheumatic type affecting the mitral and aortic valves. Syphilitic disease of the aortic valve is rarely the basis of the damage. From the irregular vegetations on the edges of the valves bacteria and emboli break off and enter the blood stream. The eye is particularly vulnerable to their attack.

The disease has an insidious onset and progresses slowly and irregularly over many months to almost inevitable death. With the signs of heart disease, there are progressive weakness, anemia, irregular elevations of temperature and the various effects of embolism. Leukocytosis, splenomegaly, clubbed fingers, petechiae and muddy pigmentation of the skin are common. There is intermittent bacteremia, with a positive blood culture at times. In over 90 per cent of cases nonhemolytic streptococci are present, usually of the viridans type. In the remaining 10 per cent the influenza bacillus, the gonococcus, Micrococcus catarrhalis, the staphylococcus and meningococcus and other organisms are encountered.

PATHOLOGIC PROCESS IN THE EYE

The pathologic changes in the eye were studied by Roth,[3] in 1872; by Herrnheiser,[4] in 1893; by Ischreyt,[5] in 1900; by Michel,[6] in 1902; by Falconer,[7] in 1909; by Dellmann,[8] in 1919; by Gilbert,[9] in 1920; by Krückmann,[10] in 1920; by Friedenwald and Rones,[11] in 1931; by Doherty and Trubek,[12] in 1931, and by Hagen,[13] in 1941. The studies before 1920 did not differentiate between the septicemia associated with subacute bacterial endocarditis and other forms of septicemia.

In the conjunctiva petechiae are common. They vary from the size of a pinpoint to that of a pinhead and are often linear. They appear in

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1. Christian, H. A.: Introduction, in Libman and Friedberg.[2b]

2. (*a*) Libman, E.: A Study of the Endocardial Lesions of Subacute Bacterial Endocarditis, Am. J. M. Sc. **144**:313, 1912. (*b*) Libman, E., and Friedberg, C. K.: Subacute Bacterial Endocarditis, New York, Oxford University Press, *1941*.

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12. Doherty, W. B., and Trubek, M.: Significant Hemorrhagic Retinal Lesions in Bacterial Endocarditis (Roth's Spots), J. A. M. A. **97**:308 (Aug. 1) 1931.

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irregular crops and last several days. These hemorrhages are readily overlooked unless searched for carefully. Iritis and iridocyclitis are rare complications.

The retinal lesions are characteristic. The retina is often cloudy, with loss of its glistening reflex. Retinal hemorrhages are common and may be round, elliptic or flame shaped. Doherty and Trubek [12] drew attention to the frequent appearance of a boat-shaped hemorrhage. Occasionally the hemorrhages have white centers called them Roth spots and described their occurrence in endocarditis. In the French literature their presence is referred to as Litten's sign. Libman and Friedberg [2b] pointed out the confusion in the use of the term "Roth spot." The error of calling a white-centered hemorrhage a Roth spot has often been made. Large retinal exudates are occasionally observed. The hemorrhages and exudates appear in crops and disappear slowly. As the fundus is observed from time to time the picture varies, with the absorp-

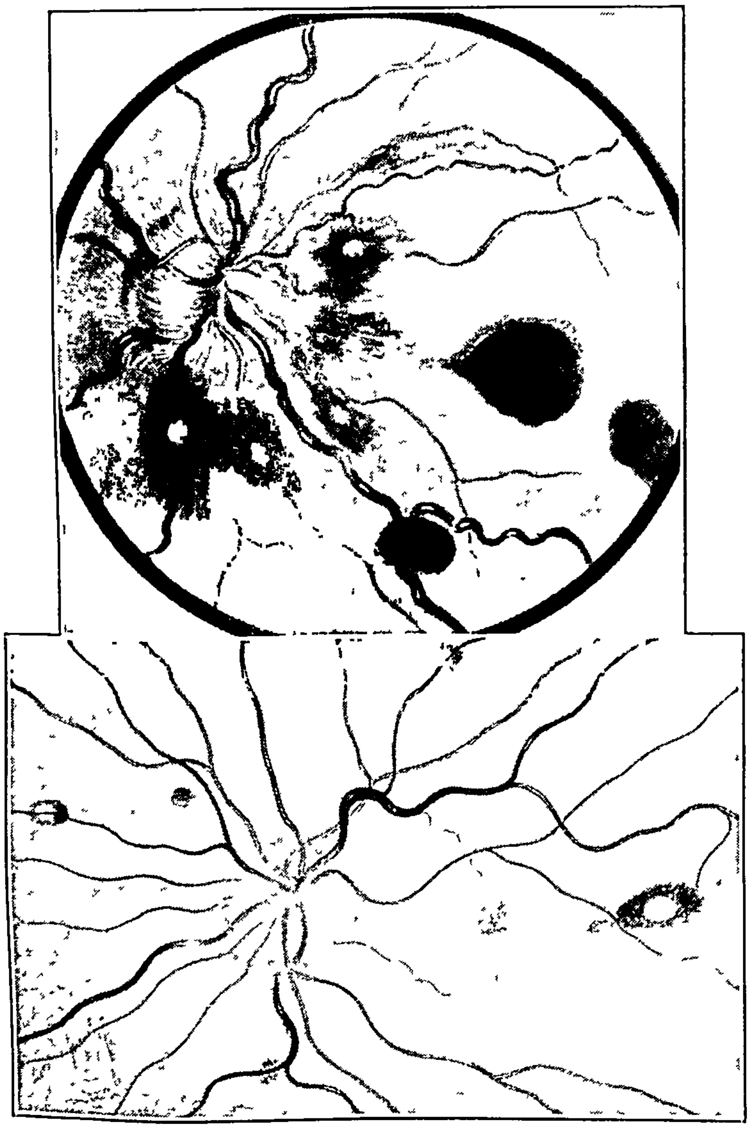

Fig. 1.—Drawings of the fundus in cases of subacute bacterial endocarditis, showing retinal hemorrhages, some of which have a white center.

which are also present in several other conditions, such as leukemia, anemia, scurvy, renal disease and sepsis. In some cases preretinal hemorrhages occur.

Small white spots in the retina are common. Such spots are also observed in other forms of septicemia. These spots were first described by Roth [3] as round white spots due to varicose degeneration of the nerve fiber layer. Litten [14] first

14. Litten, M.: Ueber akute maligne Endocarditis und die dabei vorkommenden Retinalveränderungen, Charité-Ann. 3:135, 1878; Ueber septische Erkrankungen, Ztschr. f. klin. Med. 2:378, 1881.

tion of old lesions and the appearance of new ones. Almost all patients show hemorrhages and exudates in the fundus at some time during the course of their illness.

Papillitis was observed clinically in about one third of the reported cases. Falconer,[7] in 1909, first drew attention to it. This condition is an inflammation of the nerve head, which is characteristic of subacute bacterial endocarditis and is of diagnostic significance. The disk is elevated and enlarged, and the edges are fuzzy. The veins are dilated, and the blindspot is enlarged. There is little or no visual impairment, the pres-

ence of normal vision being of diagnostic significance in cases of this type of swelling of the nerve head.

Embolism of the central retinal artery occurs occasionally and produces sudden blindness. Cerebral lesions cause various visual disturbances, the nature of which depends on their site.

The degree of anemia determines the color of the fundus. Profound anemia is common and gives a pale cast to the vessels and the entire fundus.

Examination with the slit lamp often reveals the presence of floating cells in the anterior chamber and some cells in the vitreous. Fine precipitates may be seen on the cornea. This is to be expected in view of the extensive choroidal and retinal infiltrations. We have not seen this feature reported by any other observers.

The important points in diagnosis of the ocular syndrome associated with subacute bacterial endocarditis are conjunctival petechiae; retinal hemorrhages, some with white centers; Roth spots, and edema of the disk with good vision.

Clinical Data in Five Cases of Ocular Lesions Accompanying Subacute Bacterial Endocarditis

Case No.	Patient's Initials	Sex	Age, Yr.	Ocular Changes During Life	Cardiac Lesions	Rheumatic Type	Blood Culture
1	M. F.	M	11	Papillitis; retinal hemorrhages; conjunctival hemorrhages	Mitral stenosis and insufficiency; aortic insufficiency	Yes	No growth *
2	J. M.	M	40	Not recorded	Mitral stenosis and insufficiency	Yes	Streptococcus viridans
3	E. S.	F	43	Papillitis	Mitral and aortic valvulitis	Yes	Str. viridans
4	I. L.	M	31	Papillitis; exudates in retina	Mitral regurgitation and stenosis; aortic insufficiency	Yes	Str. viridans
5	B. T.	F	44	Papillitis; retinal hemorrhages and exudates	Mitral disease	Yes	Staphylococcus aureus

* In case 1 repeated blood cultures were sterile, though autopsy showed the case to be a typical instance of subacute bacterial endocarditis.

ANALYSIS OF CASES

The pertinent clinical data in our 5 cases are outlined in the accompanying table.

The pathologic process in the eyes in these 5 cases was variable but followed a general pattern. The retina, optic nerve and choroid were most affected. During life some of the retinal lesions and the changes in the optic disk were visible, but the extensive infiltrations in the choroid were not observed and were discovered only on microscopic study.

In both the retina and the choroid the lesions were chiefly in the posterior half of the eye and were most numerous near the optic disk. This is probably accounted *for by the greater* vasculature of the posterior part of the choroid and retina. Occasional lesions extended as far as the ora serrata, and in 1 case they involved the ciliary body.

Papillitis was observed during life in 4 of our 5 cases. This is a higher percentage than other observers have noted. In the literature its presence has been reported in about one third of the cases. The degree of elevation of the disk varied from 1 to 3 D. Hemorrhages and exudates in the retina were observed during life in 3 of our cases. Pathologic study revealed their presence in 4 cases. Changes in the choroid were not detected during life but were observed in 4 cases. Infiltration of the ciliary body was not suspected during life but was revealed on microscopic examination in 1 case.

The retina in many areas presented diffuse edema with many small lesions, consisting of foci of cellular infiltrates, chiefly around blood vessels. *Most of the lesions* were in the ganglion cell and nerve fiber layers. This localization was apparently due to the origin of the infiltrations about the blood vessels, which are most numerous in these layers. Some of the larger lesions encroached on the outer layers of the *retina*, displacing the orderly arrangement of the nuclei and fibers, but rarely extended as far as the rods and cones; of the lesions that did, few reached the pigment epithelium. In 1 case a large lesion extended *through* the pigment epithelium, the lamina vitrea and the choroid and to a slight extent invaded the sclera. The type of cells in the infiltrate varied a great deal. In a few foci there were *many* polymorphonuclear leukocytes, an indication of recent and acute infection. In most lesions there were small round cells, usually with some tissue cells, *plasma* cells, fibroblasts and *endothelioid* cells, cell types indicating an older and less acute inflammation. A small number of giant cells were noted. The retina *about* the lesions was usually swollen as a result of edema.

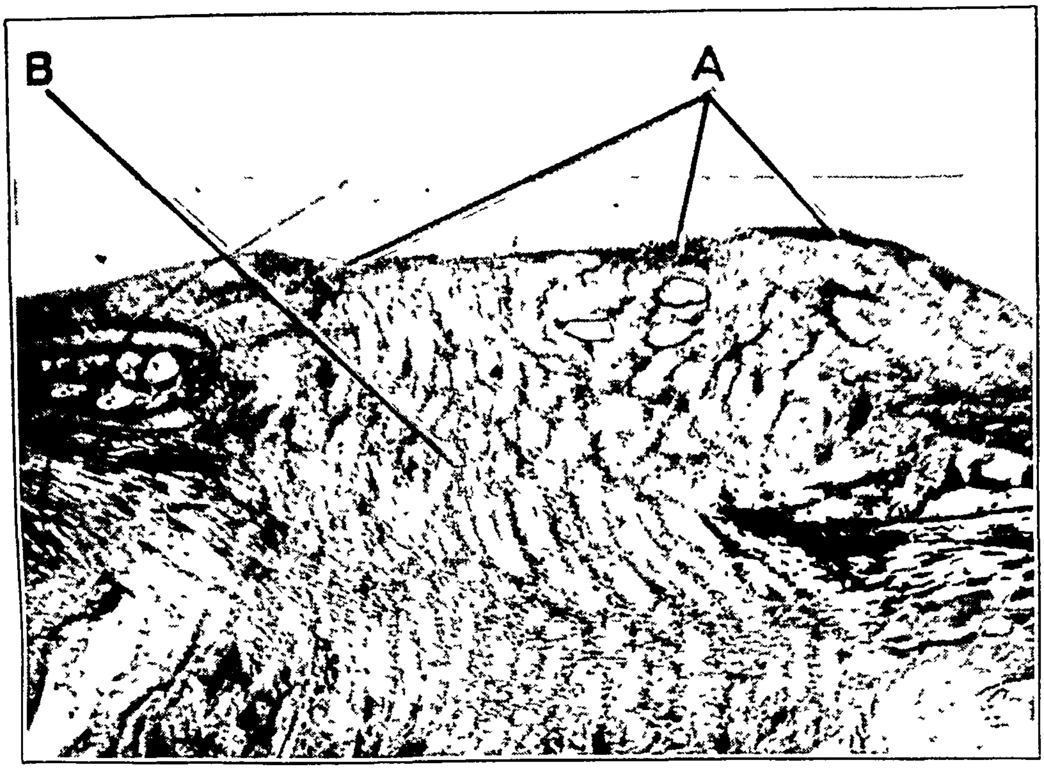

Fig 2 (case 1).—Low power magnification (× 25) of the optic nerve and optic disk, showing papillitis. *A* indicates cells forming a mantle layer; *B*, a focus of inflammatory cells.

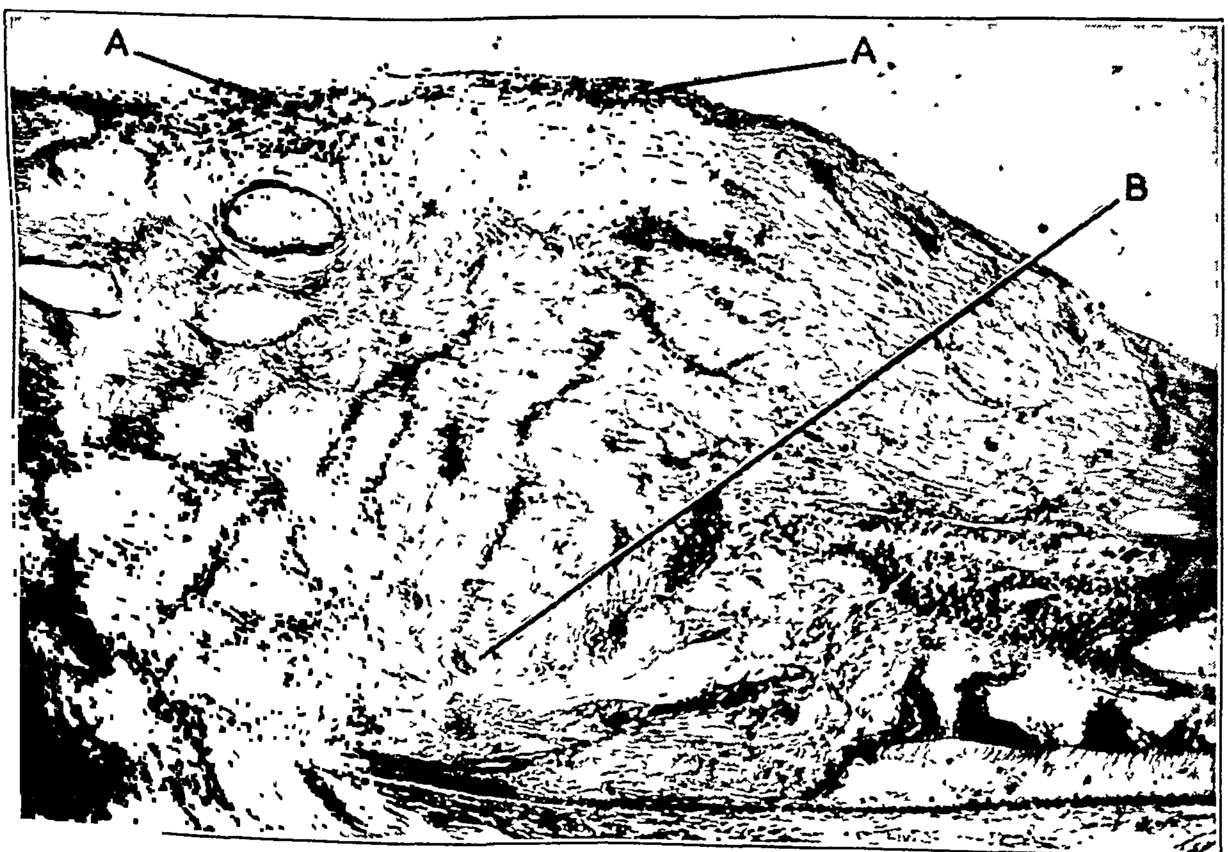

Fig. 3 (case 1).—Higher magnification (× 140) of the edge of the optic disk, showing papillitis. *A* indicates cells forming a mantle layer, and *B*, the edematous nerve, displacing the retina.

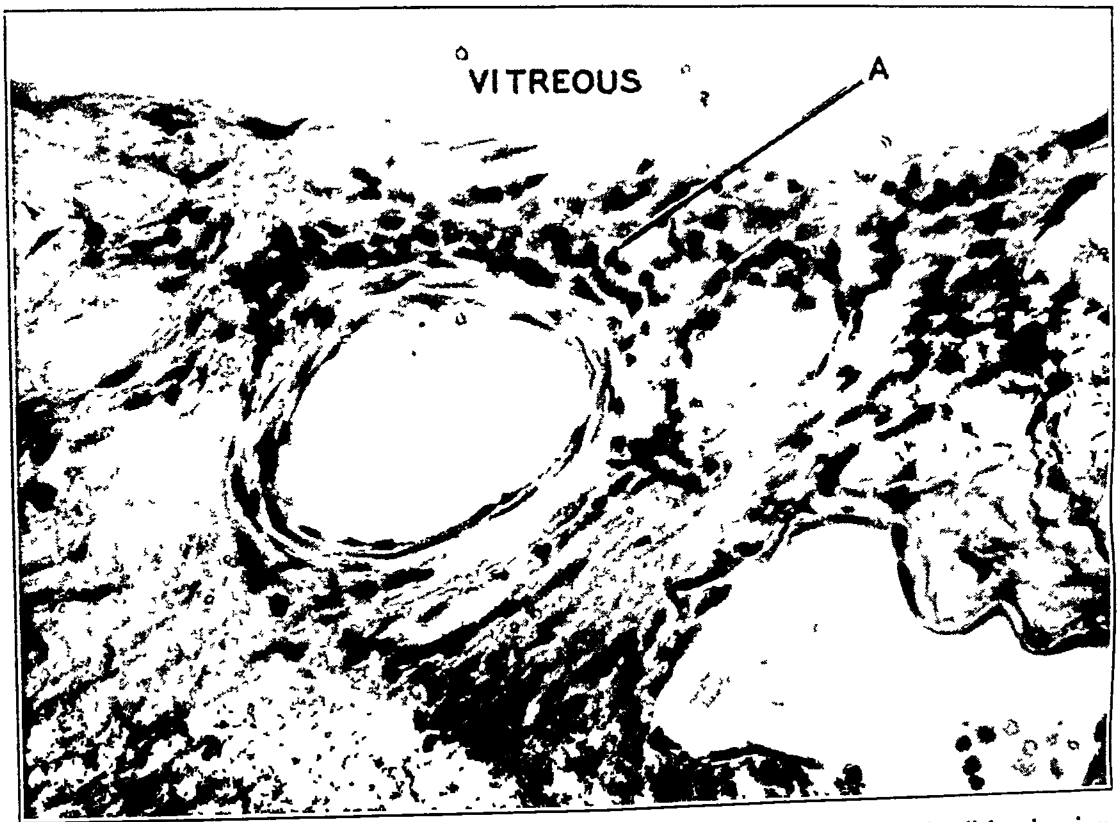

Fig. 4 (case 1).—Still higher magnification (× 308) of the surface of the optic disk, showing papillitis *A* indicates cells forming a mantle layer and surrounding the blood vessels.

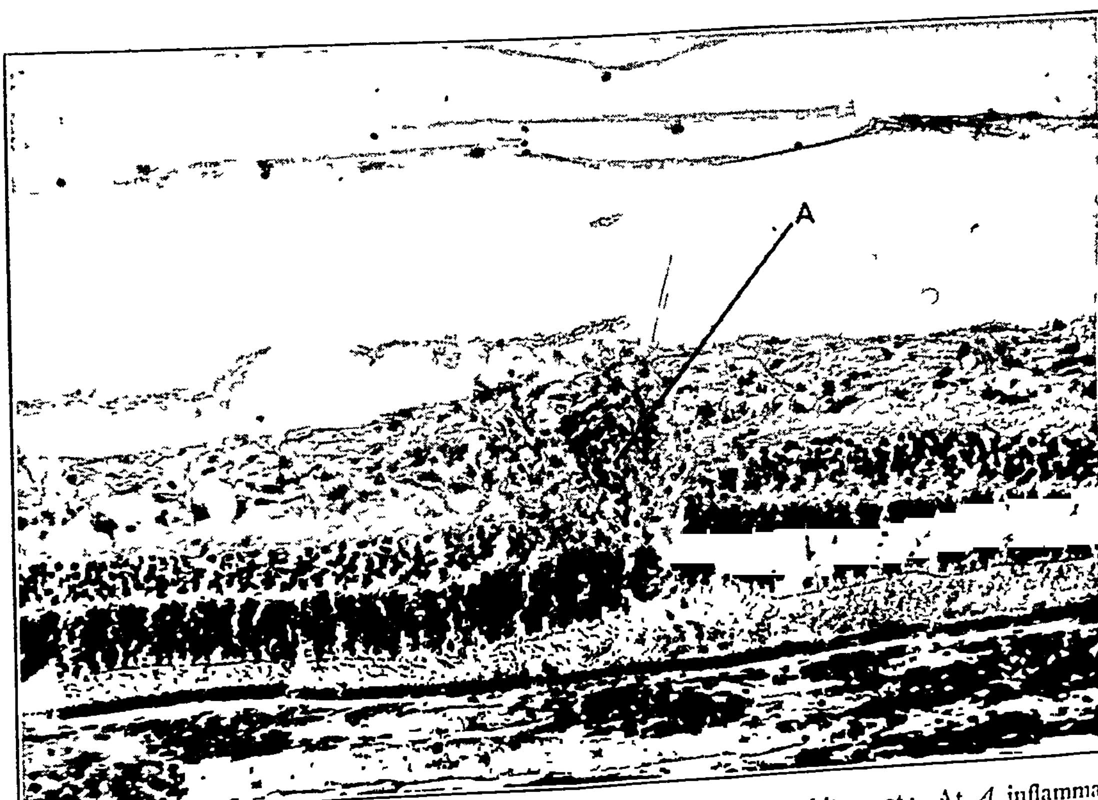

Fig. 5 (case 4).—Retinal infiltration. This area corresponds to a small white spot: At *A* inflammatory cells and edema have displaced many of the retinal elements. × 140

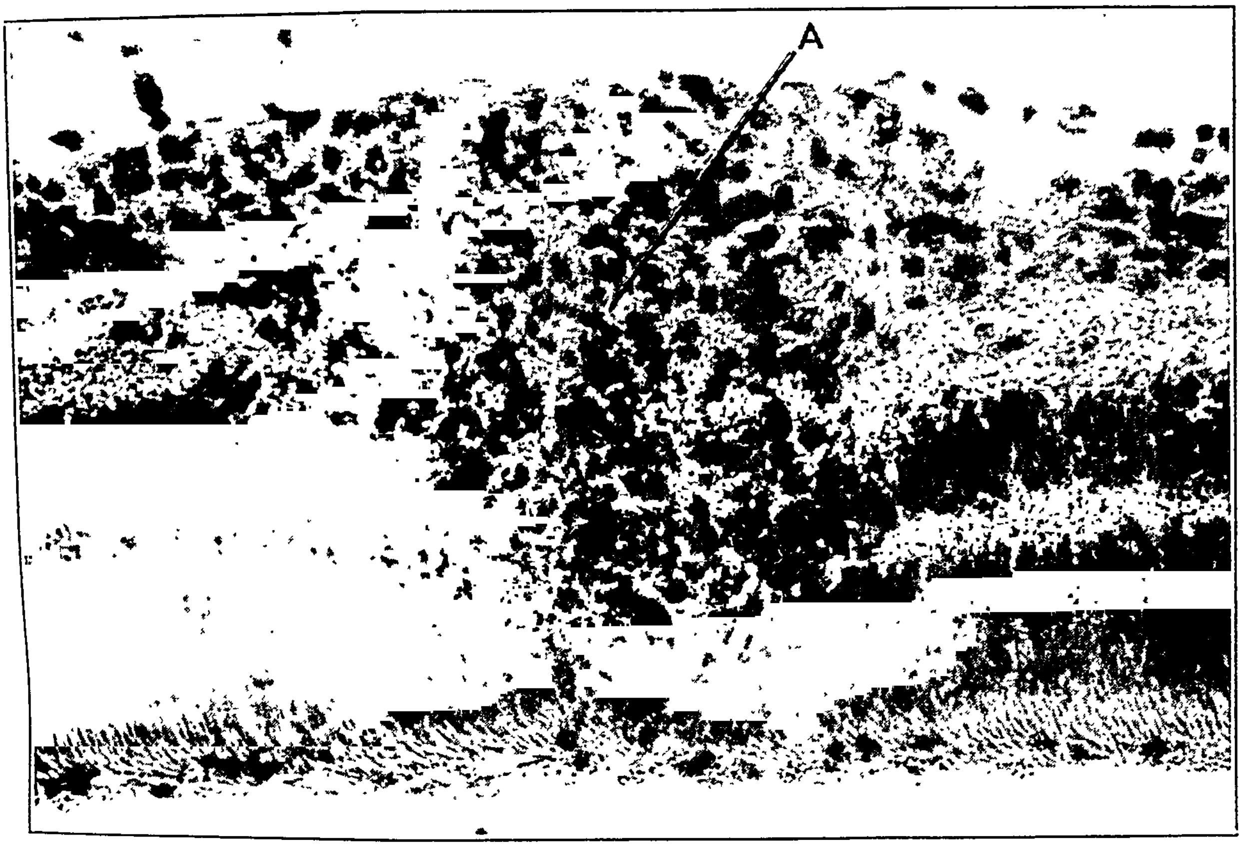

Fig. 6 (case 1).—Retinal infiltration. This area corresponds to a small white spot: At *A* inflammatory cells and edema have displaced many of the retinal elements. × 296.

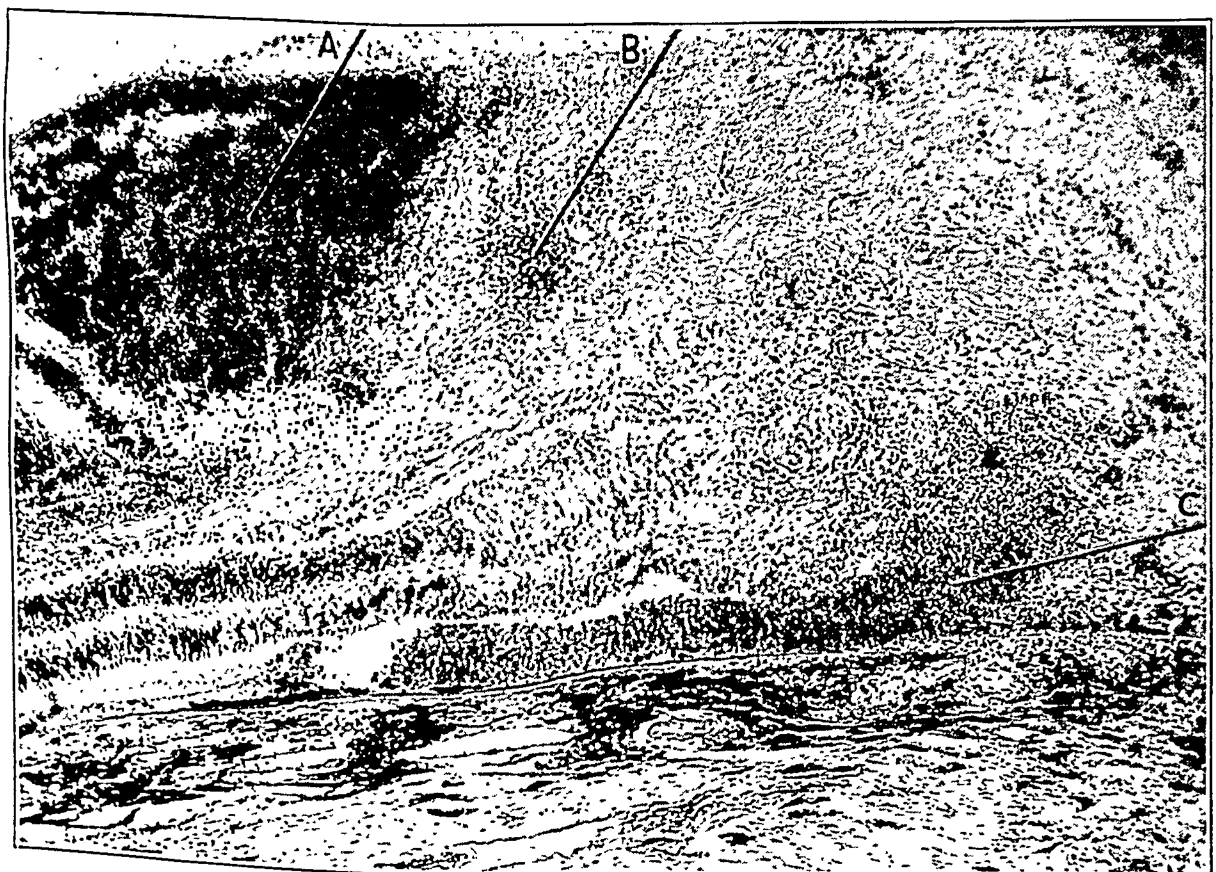

Fig. 7 (case 5).—Areas of retinal infiltration. *A*, a focus in the superficial portion of the retina; *B*, an isolated focus in the nerve fiber layer, and *C*, a lesion in the deeper part of the retina, which extends into the choroid and sclera. × 37.

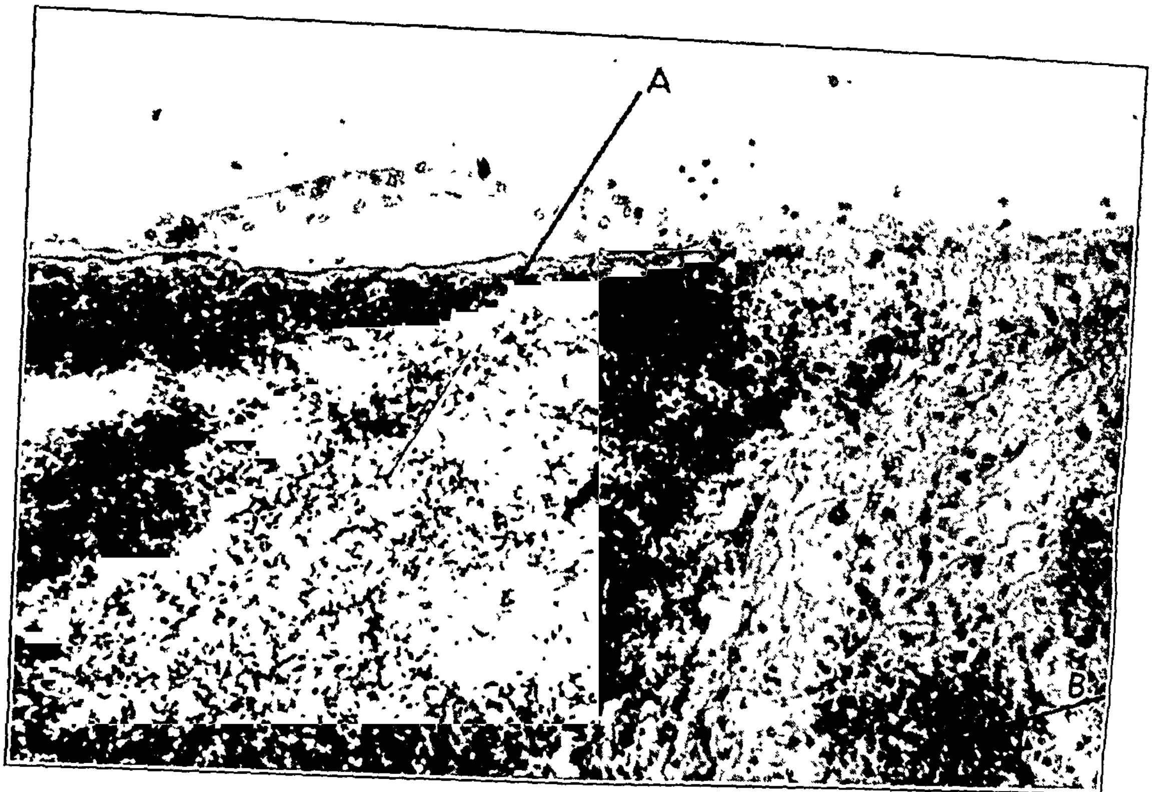

Fig. 8 (case 5).—High power view (× 153) of the area of infiltration in figure 7. The cells are densely packed. *A* here corresponds to 7 *A* in figure 7, and *B*, to *B* in the same figure.

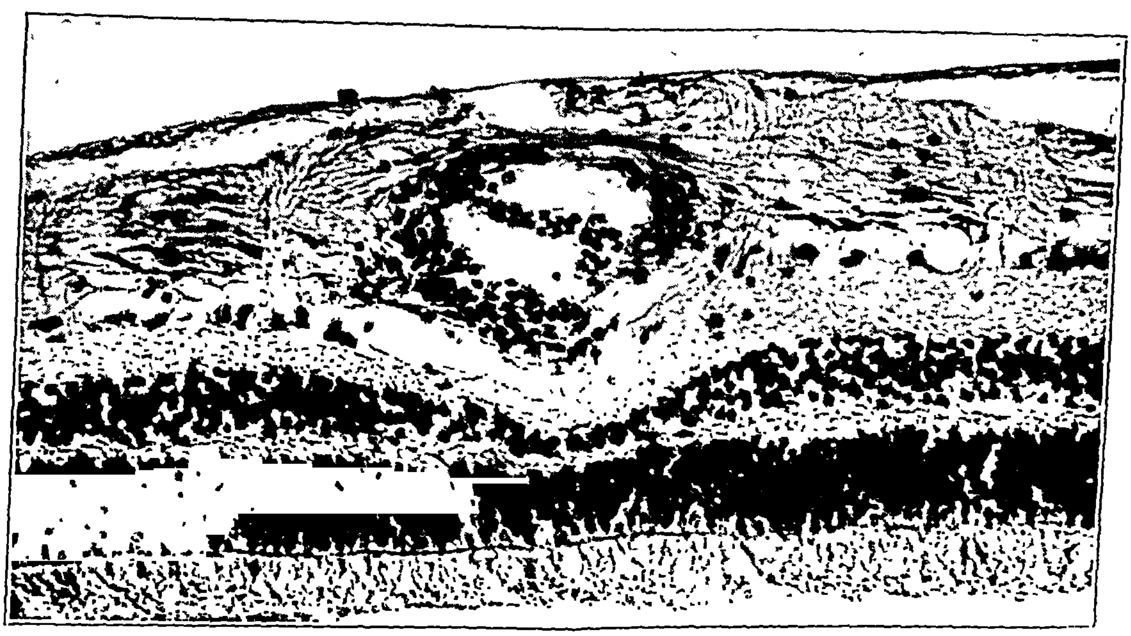

Fig. 9 (case 4).—Perivascular infiltration in the nerve fiber layer. × 147.

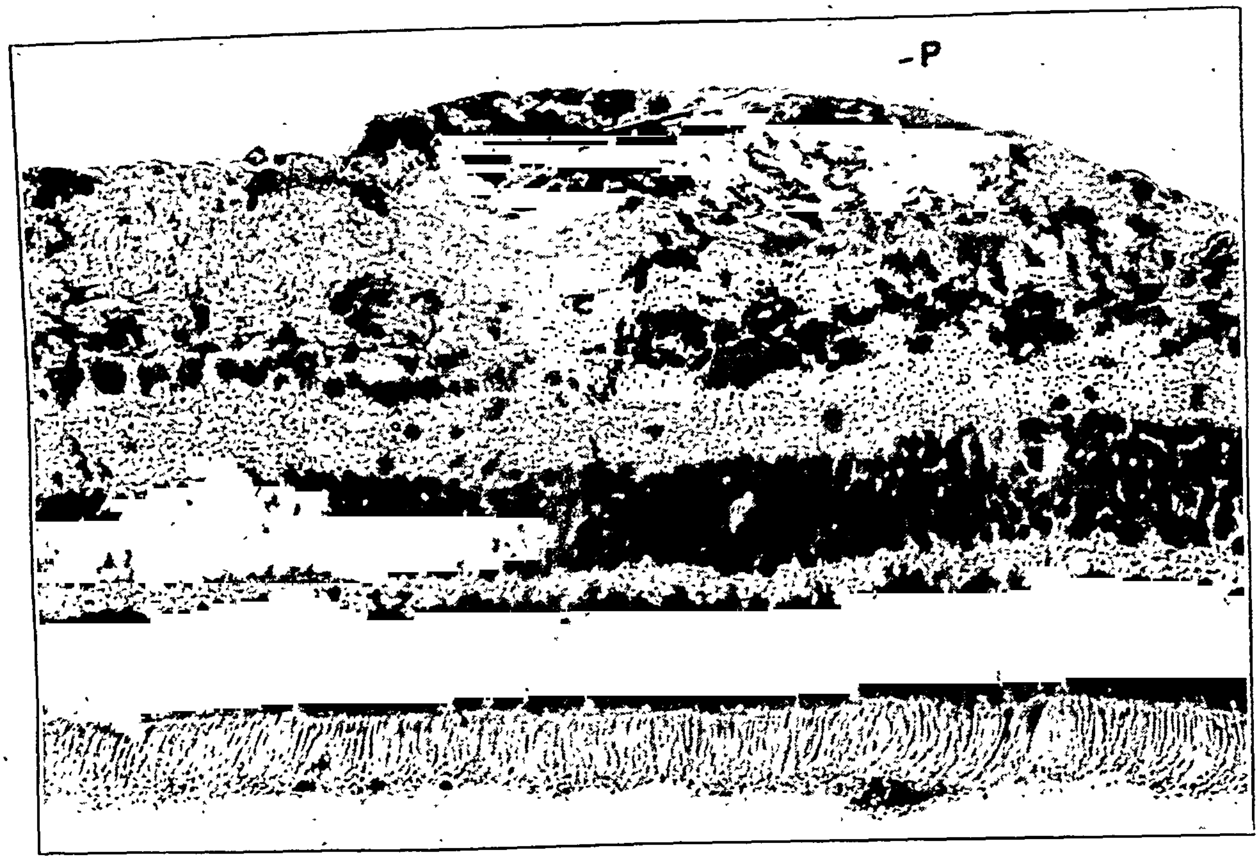

Fig. 10 (case 1).—*P*, deposit of pigment in an older retinal lesion. × 252.

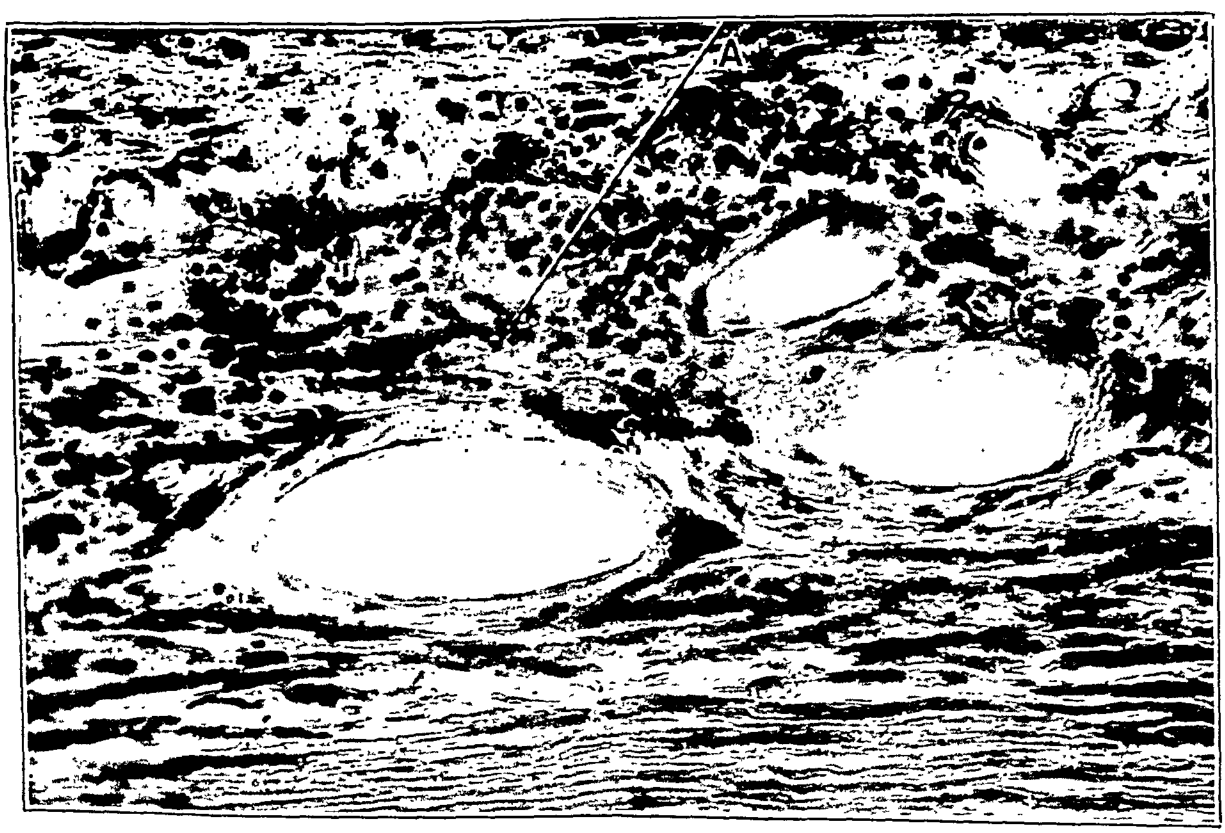

Fig. 11 (case 2).—Area of infiltration in the choroid. This is an extremely frequent lesion. At *A* a cellular infiltrate fills the space between blood vessels. × 252.

About some areas of infiltration there had been considerable diapedesis of red cells. The small foci of inflammation in the retina were numerous. In any one slide one saw several of them. In examination of the eyes during life fewer lesions were observed, as only the large, dense infiltrations were noted, while the commoner small lesions were missed.

Hemorrhages stand out against the retina during life by reason of their color. However, examination of the slides showed that there were five or six areas of infiltration for each hemorrhage seen.

A few of the older retinal lesions had irregular masses of pigment. These were probably derived from the cells of the pigment epithelium which had wandered into the retina. Doherty and Trubek [12] described areas of the retina with homogeneous, structureless changes in the nerve fiber layer, with nuclear detritus. We did not observe any corresponding lesion.

Papillitis was present in 4 of our cases. Papilledema was so intense that the surface of the disk projected into the vitreous and crowded the retina away from its edge. In addition to the edema, there were numerous small foci of new cells in the nerve and a characteristic heavy mantle layer of cells beneath the surface of the disk. The cells were of varied types; some lesions had large numbers of polymorphonuclear leukocytes, but most of them contained small round cells, some plasma cells and occasional large mononuclears, as well as rare giant cells. Most of the foci in the nerve were about small blood vessels, though a few of the larger vessels also had perivascular infiltrations. The considerable edema was apparently a reaction to the local inflammation, though it seemed excessive as compared with the small foci of cellular infiltration. Drainage of toxic products from the diseased retina and choroid into the optic nerve may have been a factor in producing the papillitis and neuritis. In 1 case there was increased intracranial pressure, which was an important factor in producing the papilledema. So the picture was one of optic neuritis and papillitis with considerable edema without loss of function of the nerve. This process differs from that of ordinary papilledema in that there is a cellular infiltration as well. It differs from optic neuritis in that there is no specific effect on the papillomacular bundle; in fact, function is little affected.

The choroid was the most extensively affected part of the eye. There were many foci of dense infiltration, chiefly of small round cells. The areas of infiltration did not appear particularly around the vessels but were between them, often arranged in rows. Most of the foci of infiltration were near the posterior pole.

Occasional cellular infiltrations were observed in the ciliary body and in the perichoroidal lamella. In a few instances small areas of infiltration from neighboring foci extended into the sclera and the subarachnoid space. We did not note any lesions in the cornea, the iris or the lens.

In the vitreous were numbers of inflammatory cells, particularly near the inflamed nerve head and the retinal lesions. These included small round cells, plasma cells and histiocytes. These foci corresponded with the cells in the anterior chamber and the fine precipitates on the posterior surface of the cornea observed with the slit lamp.

In the retina the relation of the infiltrations to the small vessels suggested that they were the result of involvement of the vessel wall, probably arteritis, from which the infection spread. In some cases they may have arisen from infected thrombi and emboli, as suggested by Friedenwald and Rones.[11]

Various names have been given this entity. In 1872 Roth [3] designated it as septic retinitis. This term, however, included cases of septicemia from causes other than subacute bacterial endocarditis. Gilbert [9] applied the name ophthalmia lenta. Friedenwald and Rones [11] included this condition under septic choroiditis. Doherty and Trubek,[12] suggested the name "retinitis of endocarditis." However, such a designation does not take into account the neuritis, papillitis and choroiditis, which are important features. This syndrome is not an isolated disease of the eye but is a manifestation of the general disease. It should be referred to as the ocular syndrome of subacute bacterial endocarditis.

SUMMARY

Subacute bacterial endocarditis often affects the eye and produces a group of characteristic signs which aid in early diagnosis. Frequent lesions are conjunctival petechiae, papillitis, Roth spots and other types of retinal exudates and hemorrhages, some of which have white centers. Examination with the slit lamp may show small floating cells in the anterior chamber and fine keratitic precipitates. The pathologic process is characterized by cellular infiltration and edema, particularly about the blood vessels in the retina and the optic nerve, and very extensive infiltrations in the choroid. Papillitis is a striking feature.

TRANSSCLERAL REMOVAL OF INTRAOCULAR FOREIGN BODY WITH THE AID OF THE BERMAN LOCATOR

HENRY MINSKY, M.D.

NEW YORK

When the anterior approach for the removal of an intraocular steel foreign body proved futile after three attempts, it occurred to me that the posterior route might be rendered less hazardous by use of the instrument which was so effective at Pearl Harbor in the hands of Moorhead,[1] for whom it had been devised to locate pieces of magnetic metal. At the suggestion of Dr. Sergei Feitelberg, of the department of physics of Mount Sinai Hospital, Mr. Samuel Berman, the inventor, demonstrated his locator.[2] Without being informed of the roentgenographic data of localization, he designated during the operation the exact spot on the sclera under which the foreign body lay.

The idea of utilizing the principles of magnetism to locate steel in the body is not new. Aveling,[3] in 1851, determined the position of needles in the soft parts of the body by using a magnetized needle suspended at its center over a suspected area. Observing that when "the magnetic indicator arrives over the part, the needle will dip and adhere to the skin, showing the exact point under which the foreign body lies," he used the method with success in 2 cases.

Thirty years later Herman Knapp,[4] evaluating the work of Pooley,[5] gave him credit for being the first to apply the principles of magnetic localization to the eye and expressed the belief that his work was of great promise. Pooley made thirteen experiments and came to the following conclusions:

1. The presence of iron or steel, if superficial and of considerable size, may be determined.

2. The presence and position of the foreign body is more easily determined if it has been previously magnetized.

3. The depth of the foreign body may be inferred from the degree of deflection of the needle.

4. A change in the position of the foreign body after the application of the magnet may be ascertained.

Pagenstecher,[6] in the same year, without knowing of Pooley's work, conducted similar experiments and obtained the same results. In 1894 Asmus [7] described his *Sideroskop,* in which a mirror reflected the excursions of a magnetic needle onto a scale. The instrument evidently proved inadequate since it never became popular, although von Blaskovics and Kreiker [8] mentioned its use in their differentiating a magnetic from a nonmagnetic foreign body.

With the development of Berman's metal locator, Knapp's prophecy is materialized in an instrument which I believe helps to make the posterior approach to the removal of an intraocular foreign body less formidable than heretofore.

The locator operates in the following way:

In a diagnostic rod is placed the equivalent of two transformers—one in the handle and the other at the tip, which is used to search for the foreign body. The primary coils are connected in series to a source of alternating current. Also in series, the secondary coils are connected through an amplifying unit to a voltmeter. When an alternating current is sent through the primary coils, a current is produced in the secondary coils by induction. The instrument has a means of equalizing (balancing out) the voltages in the secondary coils so that the needle of the voltmeter will read

This paper was read at a meeting of the Section on Ophthalmology, New York Academy of Medicine, Dec. 20, 1943.

1. Moorhead, J. J.: A Foreign Body Finder: The Locator, J. A. M. A. **121**:123 (Jan. 9) 1943.

2. Waugh Laboratories, 420 Lexington Avenue, manufactures the locator.

3. Aveling, J. H.: On the Detection by the Aid of Magnetism of Needles Embedded Near the Surface of the Body, Lancet **1**:149, 1851.

4. Knapp, H.: Removal of Fragments of Iron from the Vitreous, Arch. Ophth. **9**:207, 1880; Zwei Fälle von Extraction von Eisenstückchen aus dem Glaskörper, Arch. f. Augenh. **10**:8, 1881.

5. Pooley, T. R.: On the Detection of the Presence and Location of Steel and Iron Foreign Bodies of the Eye by the Indication of a Magnetic Needle, Arch. Ophth. **9**:256, 1880; Der Nachweis und die Localisation von Stahl-und Eisenpartikeln im Auge durch die Indicationen der Magnetnadel, Arch. f. Augenh. **10**:9, 1880.

6. Pagenstecher, H. T.: Two Cases of Extraction of Iron from Vitreous, with Observations on the Diagnosis and Extraction of Steel and Iron Particles by Means of the Magnet, Arch. Ophth. **10**:145, 1881; Zwei Fälle von Extraction von Eisenspaltern aus dem Glaskörper, nebst Bemerkungen über die Diagnostik und Extraction von Stahl- und Eisenstückchen vermittelst des Magneten, Arch. f. Augenh. **10**:234, 1881.

7. Asmus, E.: Das Sideroskop; ein Apparat zum Nachweis der Eisen-und Stahlsplitter im Inneren der Augen, Arch. f. Ophth. **40**:280, 1894.

8. von Blaskovics, L., and Kreiker, A.: Eingriffe am Auge, Stuttgart, Ferdinand Enke, 1938, p. 438.

approximately zero, since no current flows between them. fundus and reduced vision to the perception of hand move-

the upper temporal quadrant of the orbit. With the hypodermic needle piercing the conjunctival surface of the external canthal ligament to reach the periosteum over the anterior surface of the external bony margin of the orbit, 2 cc. of 4 per cent procaine hydrochloride was injected. Akinesia of the lids was produced.

Exposure of Sclera: The sclera was exposed in the upper temporal quadrant, as in the operation for replacement of a detached retina. The conjunctiva and Tenon's capsule, as one layer, were opened 15 mm. from the limbus, after the speculum was inserted. The anterior flap was dissected down and laid on the cornea. Catgut retraction sutures were placed in the posterior flap as far from the free edge as possible by previously picking up Tenon's capsule in the depths. When these sutures were drawn up toward the brow and anchored on the forehead after removal of the speculum, the posterior attachment of Tenon's capsule caused the eyeball to rotate downward and expose the posterior aspect of the sclera.

Berman Locator: The tip of the Berman locator, in a sterile rubber jacket, was moved on the surface of the sclera while the needle on the indicator scale was watched for its greatest amplitude. Since the needle went beyond the markings on the scale, the current was reduced in order to have the needle poised at about two-thirds the length of the scale. When the site of the foreign body was found, its position was checked by the operator's moving the locator and observing that the needle read less and less. After the locator was returned to the spot where the needle resumed its first position, a black silk marking suture was placed there in the episclera. Along the meridian of this locating suture, another silk suture was placed in the episclera just beyond the limbus, for purposes of retraction.

Scleral Flap: With a Knapp needle knife, a semicircular incision was made 3 mm. away from the marking suture. The incision was beveled so that the opening into the suprachoroid space would correspond to the diameter of the semicircle in the sclera. In this case the opening was made parallel with the limbus. It might be better to have it fall in a meridional direction so as to avoid any possible injury to a ciliary vessel or nerve. After the scleral flap was raised, the incision was continued until a black chink of choroid showed through the innermost scleral fibers. The remaining scleral fibers were stripped with the closed points of the Stevens scissors until 2 mm. of choroid was plainly visible. The scleral flap was then raised higher, and one blade of the Stevens scissors was inserted in the suprachoroid space to enlarge the scleral opening on each side so that the foreign body might be easily delivered.

Microcautery Barrage: The scleral flap was allowed to fall in place, and a barrage of seven electrocoagulation cautery punctures was made with the Kronfeld needle, 5 mm. apart, in a circle 10 mm. in diameter around the marking suture. These punctures were made obliquely in the sclera so that they just touched the choroid and avoided entering the vitreous.

Placement of Scleral Sutures: Three catgut sutures were placed in the lips of the scleral wound but were left untied The loops of the sutures were drawn away from the wound so as not to interfere with the next step.

Removal of Foreign Body: The broad tip of the hand magnet was placed on the posterior scleral lip after the scleral flap was lifted. When the current was applied, the choroid rose toward the tip, proof that the foreign body was present in the area exposed. The choroid and retina were then seared by the flat surface of the Kronfeld needle along the length of the wound. With the current on, the point of the needle gently tore through the coagulated tissue, exposing the hyaloid membranes. No bleeding occurred. A smaller tip was placed on the hand magnet and applied to the opening. The foreign body, 3 mm. long, 1.5 mm. broad and 0.5 mm. thick, appeared on the tip of the magnet after the second application of current. The small head of the vitreous which appeared was cut off flush with the wound, and the scleral sutures were tied promptly. The retraction and marking sutures were removed, and the conjunctiva and Tenon's capsule, as one layer, were closed with interrupted catgut sutures. After a 3 per cent solution of atropine sulfate had been instilled and both eyes closed with a light dressing and mask, the patient was placed in bed on his left side, with the foot of the bed raised.

Postoperative Course.—Two days after the operation the patient received a drop of a 3 per cent solution of atropine sulfate, which procedure was repeated daily for a week. Then he wore pinhole glasses and was placed under a regimen of hot compresses and instillation of 1 per cent atropine sulfate three times daily. He was given an intramuscular injection of 10 cc. of boiled milk every three days for five doses. Between injections he received large amounts of salicylates. Three weeks after the operation he was discharged, with the eyeball fairly white and the cornea clear except for a through and through scar, which could be easily seen at 11 o'clock. No precipitates were discernible on the posterior surface, although the posterior synechiae were still present at 11 o'clock. The anterior portion of the lens was clear. While the posterior subcapsular clouding was conspicuous, it seemed much clearer than before the operation when viewed with the ophthalmoscope. Through a clear vitreous, the fundus showed the scars of chorioretinitis resulting from the coagulating tear and the barrage of cautery punctures. Six weeks after the operation vision was 16/50 with a + 1.50 D. sphere. Three months later the vision was 20/40 —.

COMMENT

It is assumed that before the posterior approach is resorted to attempts at removal of an intraocular foreign body by the anterior route have proved futile. Gulliver [9] recently pointed out that he almost never had to use the transscleral technic to remove an intraocular foreign body. Spaeth [10] stressed the dictum that "a foreign body should not be removed through a posterior sclerotomy unless it is absolutely necessary because of the fear of secondary detachment of the retina occurring in a very high incidence of cases." He strongly condemned the practice of introducing magnet points or magnetized instruments into the vitreous in the search for a foreign body and insisted on a barrage of microcautery punctures, similar to those employed when an ordinary separation hole is under treatment.

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9. Gulliver, F. D.: Particles of Steel Within the Globe of the Eye, Arch. Ophth. **28**:896 (Nov.) 1942.

10. Spaeth, E. B.: Principles and Practice of Ophthalmic Surgery, Philadelphia, Lea & Febiger, 1939, p. 801.

The success of the posterior approach depends on the scleral incision's being as near the foreign body as possible. It is perhaps well to realize that in the roentgenographic estimation of the position of an intraocular foreign body the factor of error ranges between 5 and 10 per cent.[11] This error is increased when it become necessary to use calipers, protractor, millimeter rule and meridional angles to mark a point on the sclera corresponding to the plotting on a chart. It seems to me that the risk of the scleral incision's being misplaced is considerably reduced, if not entirely eliminated, by employment of the Berman locator as a check on the roentgenographic localization.

The four claims that Pooley[5] made for the use of a magnetic needle seem to be even more justified for the locator because the perfected instrument can be used with such ease. Furthermore, if roentgenographic localization is impossible or, as in my case, not immediately available, much time is saved by use of the locator at once. In cases in which the differential diagnosis of a foreign body in the eye and one just outside of the sclera is difficult, the problem could easily be resolved by the locator once Tenon's capsule was opened.

11. Schwartz, I.: Personal communication to the author.

This single, relatively incomplete case history is reported so that the use of the Berman locator may be brought to the attention of the ophthalmic surgeon, inasmuch as there is to be expected an increased incidence of ocular injuries, due both to the war and to the increased tempo of industrial activity. The technic described here gives the promise of a better prognosis for the removal of an intraocular foreign body by the transscleral route.

DISCUSSION

Dr. Elbert S. Sherman, Newark, N. J.: One naturally wonders why the foreign body was not removed immediately by the transscleral route.

Dr. Henry Minsky: Dr. Sherman's criticism is justified. I tried on three successive days to remove the foreign body by the anterior route because I thought the transscleral route more hazardous. With my limited experience with intraocular foreign bodies, I preferred to work through the silent area, just behind the ora serrata, where there seemed to be less likelihood of producing a subsequent detachment of the retina. I feel that the operation should always be done as soon as the diagnosis is made. Now, with roentgenographic localization, aided by the Berman locator, I think that the transscleral route is as safe as the anterior route, perhaps more so. The danger of detachment of the retina can be prevented by the procedure already described.

2 East Ninety-Fifth Street.

EMERGENCY ROOM SERVICE AT WILLS HOSPITAL

ROBERT E. SHOEMAKER, M.D.
Resident Surgeon, Wills Hospital
PHILADELPHIA

This survey of the emergency room cases at Wills Hospital was originally undertaken to determine the relative value of the service in experience and training to the resident surgeon. The study serves the additional purpose of recording the incidence and type of the so-called accident ward cases of a specialized hospital and may perhaps be of value from the standpoint of teaching.

INSTITUTION AND LOCALITY

The Wills Hospital at present is the largest hospital in the United States devoted entirely to diseases of the eye. Its annual rate of admission of inpatients is 3,624, and the admissions to its outpatient clinics number approximately 132,000 each year, of which 32,000 represent new cases.

The city of Philadelphia is the third largest in the country, with a population of 1,950,961 in 1930 and of 1,931,554 in 1940. With the onset of the present war and the tremendous increase in heavy industry, the estimated population as of December 1942 was 2,262,693, a relative increase of about 15 per cent in the past two years.

There are about forty general hospitals, large and small, in the city, in the accident wards of which many ocular conditions are seen. The larger industrial plants have their own medical departments. Obviously, the incidence at Wills Hospital does not suggest the total number of ocular emergencies in metropolitan Philadelphia, but it may be accepted as a relative indication of both number and type.

The following figures indicate the increase in admissions to the emergency room in the past five years.

Year	Nonindustrial Patients	Industrial Patients	Total No. of Patients
1938	4,135	874	5,009
1939	4,600	1,043	5,643
1940	4,763	1,263	6,026
1941	5,436	1,875	7,311
1942	5,811	2,719	8,530

As was to be expected, the increase in ocular emergencies since 1940 was relatively much greater among the purely industrial cases. This agrees with the fact that in Philadelphia the increase in population represents largely an increase of workers in war industries.

METHOD

Since over a period of time each resident physician at Wills Hospital spent the equivalent of twenty-four hours daily for two months in the emergency room service, each of the six residents attended approximately 1,422 patients during 1942. To provide a fair sample, 1,422 consecutive emergency room records were inspected in alphabetic order and the data tabulated. If several conditions were present, only the one considered of primary clinical importance was listed.

Obviously, in such a survey there is a certain inaccuracy. The patients seen in the emergency room during the course of the year were attended in greater or lesser numbers by eight residents. A condition, for example, which one physician would consider as necessitating the patient's referral to the clinic might not be so considered by another. However, all persons concerning whom there was doubt as to the diagnosis or the disposal of the patient were referred to the senior resident.

DATA AND COMMENT

Age Incidence.—The greatest incidence of ocular emergencies was in the third, fourth and fifth decades, i. e., between the ages of 20 and 50 years (fig. 1). This is obvious with respect to the incidence for outside and industrial workers. Among nonindustrial workers, the efficiency of the protective mechanism of the eye, the good general ocular health and the absence of degenerative changes during the first two decades of life probably explain the lowered incidence during childhood, even though children spend a good part of their time out of doors. With advancing years the reversal of these conditions becomes an important factor, and so persons in the sixth and seventh decades are seen just as often in the ophthalmic service, even though they are less likely to receive ocular injuries.

Sex Incidence.—Of the total number of patients, 336, or 23.6 per cent, were females. At present women in war industries are subjected to and are receiving the usual industrial injuries to the eyes. Nevertheless, industry has not as yet been responsible for any great increase in the number of females seen.

Seasonal Incidence.—Again, as was to be expected, there were a general decrease in patients seen during the cold weather months, with fewer people on the streets, and a general increase during hot weather, with more people out of doors, both night and day. The winds of March and

April did not produce a peak in the incidence but may have had a part in the general upswing. The incidence of industrial cases is normally little affected by season.

Origin (either recorded or inferred).—The injury was sustained at home by 58 patients, on the street by 525 patients and at work by 467 patients.

Inflammatory and nontraumatic conditions, except for traumatic ulcer and conjunctivitis, were not included in these figures. The relatively large number of patients who received a foreign body in the eye while at work is of interest.

The Eye Involved.—The right eye was involved in 651 patients; the left eye, in 601 patients, and both eyes, in 170 patients.

Although the series is small, it may be significant that the right eye was more often involved (8 per cent). The right eye, being more often dominant, is more likely to be the eye used, for example, when one is looking upward through a tube sight or to be kept open when one is squinting hard to avoid wind-blown dirt, and so it probably is more likely to receive a foreign body.

Diagnosis (in general listed in order of frequency).—A. Traumatic and Noninflammatory Conditions of the Eye: The conditions encountered, with their incidence, are tabulated as follows:

Condition	No. of Patients
Foreign body	697
Cornea	507
Upper lid	95
Bulbar conjunctiva	80
Lower lid	13
Intraocular	1
Lens	1
Foreign body suspected but not found	32
Traumatic conjunctivitis	101
Abrasion of cornea	89
Photophthalmia (such as welder's flash)	38
Burn of cornea or conjunctiva	41
Chemical	15
Thermal	26
Contusion of globe	20
Subconjunctival hemorrhage, spontaneous	16
Laceration of cornea, conjunctiva or globe	12
Laceration of lids or orbit	7
Perforation of cornea	4
Traumatic hyphemia	3
Traumatic cataract	2
Perforation of globe	2
Abrasion of conjunctiva	2

A comment here is necessary to account for the relatively small number of patients with intraocular and intraorbital foreign bodies. Most of the patients sought relief on their own initiative, as suggested by the fact that the largest percentage reported in the afternoon and the early evening, i. e., after working hours and at a time which was most convenient to them. Intraocular foreign bodies, even if only suspected, are usually the result of a major accident and demand more than casual attention. Hence patients with such injuries are usually received at the admission desk of the hospital accompanied by a letter from a physician, from the medical department of an industrial plant or from an insurance company addressed to a specific attending surgeon—in this respect being quite different from patients with the other conditions.

B. Inflammatory and Nontraumatic Conditions: The disorders of this kind, with their incidence, are tabulated as follows:

Condition	No. of Patients
Conjunctivitis, acute and chronic	169
Corneal ulcer	33
Nonulcerative keratitis	20
Iritis, iridocyclitis and uveitis	20
Chalazion	16
Hordeolum	13
Dacryocystitis	9
Acute inflammatory glaucoma	6
External infection of lids or orbit	6
Episcleritis	4
Epiphora (cause not stated)	4
Dermatitis of lids	4
Obvious refractive error	4
Concretions of lids	4
Trichiasis	4
Blepharitis	3
Sudden amblyopia	3
Onset of squint	3
Angioneurotic edema	2
Tumor of lids	2
Insect bite	2
Panophthalmitis	1
Undiagnosed condition	8
Miscellaneous conditions	24

There were three times as many patients with traumatic and noninflammatory disorders as those with inflammatory and nontraumatic conditions. This is to be expected. Almost half the patients came to the emergency room because of a foreign body in the eye.

The service was characterized by a definite increase in the incidence of industrial foreign bodies and of conjunctivitis. The cases of conjunctivitis included the usual types and, in addition, a type related to the epidemic keratoconjunctivitis of virus origin reported in the literature, although few of the patients when first seen had the reported corneal lesions or the adenopathy.

The large number of patients with foreign bodies emphasizes the attention that must be paid to training in the proper means and methods of removal. The great variety of conditions encountered suggests the ophthalmologic background that must be acquired.

Disposition of Patients.—In this series, 726 patients were referred to a clinic or a private physician and 26 patients were admitted to a hospital.

The diagnoses on admission to Wills Hospital were as follows: acute glaucoma, 4 patients; perforating wound of the cornea, 3 patients;

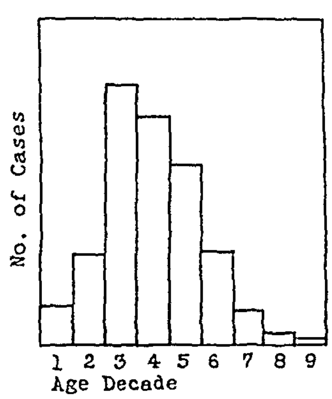

Fig. 1.—Age incidence in a resident physician's sample of emergency cases at Wills Hospital for 1942.

perforation of the globe, 2 patients; traumatic cataract, 2 patients, and laceration of the globe, lime burn of the cornea, retinal detachment, commotio retinae, burn of the cornea, severe keratoconjunctivitis, deep foreign body in the cornea, traumatic hyphemia, intraocular foreign body, congenital cataract and panophthalmitis, 1 patient each. The remaining 4 patients were referred to other hospitals for admission, with the following diagnoses: apoplexy with amblyopia, laceration of the head, human bite of the orbit and possible fracture of the skull.

Over half the patients seen were indirectly referred; although this is possibly a large number, any error is on the safe side.

There was a certain variability in the disposal of the patients. For example, a patient with glaucoma seen in the early morning might be placed under routine treatment, to be admitted by the clinic if necessary that afternoon. Or a patient with a burn of the cornea might be given emergency treatment and referred to the clinic for decision as to his possible admission. Furthermore, all patients with injuries involving compensation were referred to the company ophthalmologist if admission was not urgent. Patients with burns, for example, might be admitted later through the company physician to this or to another hospital.

In view of the high incidence and the relative importance of foreign bodies of the cornea, a brief comment on the technic of removal of such bodies of the cornea as practiced in the emergency room at the Wills Hospital may be of interest.

The patient is seated in a chair the back of which rises about 6 inches (15 cm.) higher than the average patient's head. The physician stands by the patient's left shoulder, his right arm resting on the top of the chair and directed down over the patient's head, with the base of the right hand resting on the upper part of the forehead. This provides a controlling support for the arm and hand and leaves the thumb and the first two fingers free to hold the foreign body spud, while the ring and little fingers are used to elevate and fix the upper lid. The thumb and the first two fingers of the left hand hold a condensing lens, while the two remaining fingers are used to depress and fix the patient's lower lid and, at the same time, provide support for the left hand.

Illumination is provided by means of a Bausch and Lomb ortholite lamp placed about 1½ feet (45 cm.) in front of the patient and slightly to his right. The light is then focused and controlled by the condensing lens in the physician's hand to provide direct illuminating retroillumination or sclerotic scatter in a manner similar to that employed with the slit lamp. This is of practical importance, since some foreign bodies are made more readily visible by retroillumination, while others, especially small fragments, are more easily demonstrated by sclerotic scatter. The advantages of controlled illumination and support for the operating hand are of considerable importance, and it is only in the exceptional case that the aid of the slit lamp is actually demanded for removal of the foreign body.

The foreign body spud is of interest. One end is fashioned like a dental burr, so that the physician has

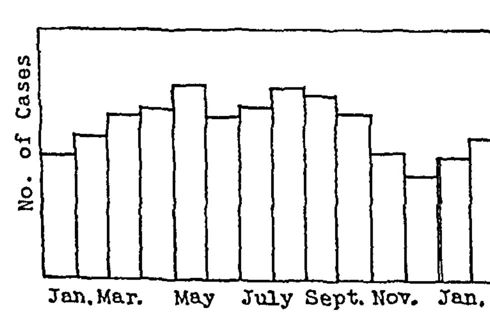

Fig. 2.—Seasonal incidence in the sample of 1,422 emergency cases at Wills Hospital for 1942.

merely to reverse the instrument in order to burr out a rust ring or to smooth a ragged surface.

Tetracaine hydrochloride, in 1 per cent solution, is employed as a local anesthetic and may be ordered for the patient's use at home if the eye is painful, especially when there has been loss of corneal surface. In the latter case, after instillation of an antiseptic-analgesic ointment to relieve discomfort, a patch is placed over the eye, so that the lid may act as a splint to favor healing.

Atropine or homatropine is usually instilled when the patient comes to the emergency room with a ciliary flush or when the operative trauma is excessive.

Wills Hospital.

ARIBOFLAVINOSIS AS A PROBABLE CAUSE OF VERNAL CONJUNCTIVITIS

LUIS CASTELLANOS A., M.D.

CHIHUAHUA, MEXICO

Vernal conjunctivitis was first described in 1846 by Arlt, who called it a variety of eczematous conjunctivitis. Vernal conjunctivitis is a chronic disease, of many years' duration. During the winter little disturbance is experienced, while with the beginning of the spring heat the eyes become reddened and photophobia and, above all, a great deal of itching of the eyes occur. The objective changes are presented in the tarsal conjunctiva and in the sclerocorneal limbus and its vicinity, while the rest of the bulbar conjunctiva and the fornix are normal.

In cases of the mild form the tarsal conjunctiva shows a white velum, or there is permanent hyperemia of the scleral conjunctiva, with ciliary injection; with the more acute form the tarsal conjunctiva is hypertrophied, with the formation of enlarged and flattened papillae, so that the surface has a cobblestone appearance. The changes in the limbus consist of pale, grayish red, uneven nodules of gelatinous aspect, in which are noted small, white, calcareous-looking dots (Trantas' dots). As a rule these lesions appear on the nasal or the temporal aspect of the limbus in the interpalpebral area. They extend little by little into the cornea. The change at the margin of the cornea consists in proliferation of the conjunctival epithelium, with hypertrophy of the underlying connective tissue. This gives rise to the large, reddish gray prominences, which may surround the entire cornea. The tarsal conjunctiva around the diseased area is thickened, and its papillae are enlarged and present a characteristic mamillated appearance.[1] The vessels which pass over the elevations are dilated; the cornea remains transparent, and only at times a vague annular opacity, parallel with the edge of the elevations, may be seen. In this advanced stage the objective appearance changes little in any season of the year in which the patient may be examined, except that the eyes are paler in winter and more injected in summer.

Vernal conjunctivitis is not rare and generally affects males. It is essentially a disease of childhood and adolescence; both eyes are generally attacked, and as a rule the disease recurs annually for years (three, four or even twenty), when it finally disappears, leaving no trace. It is only seldom that one sees the more advanced form. Usually this stage is characterized by the subjective symptoms of itching, a sensation of heat or of a foreign body (as of dust) in the eyes and mild photophobia. The tarsal conjunctiva is congested. Histologically the condition is characterized by hyaline degeneration of the subconnective tissue and the presence of numerous eosinophil cells in the secretion, which is rarely present.

ETIOLOGIC CONSIDERATIONS

Kreibich and Dimmer expressed the opinion that vernal conjunctivitis is caused by solar rays and they compared it with other dermatoses of the same origin. Other authors have attributed it to various conditions such as hay fever and anaphylaxis; generally the cause is stated to be unknown.

I believe the cause of this disease is a deficiency of riboflavin, the deficiency being due to more rapid destruction of the vitamins by the ultraviolet rays of sunlight or to the demand for a greater quantity of this vitamin during the hot season. I base this affirmation on the results I have obtained in the treatment with riboflavin of 105 patients, 92 per cent of whom showed immediate improvement in their condition. Since this disease lasts a number of years, it is as yet impossible for me to present definite conclusions with regard to the value of this therapy, but in view of the results I have obtained there is strong evidence that a deficiency in riboflavin is the cause of vernal conjunctivitis.

Pellagra is due to a deficiency of another component of the vitamin B complex, nicotinamide, or the P-P factor; it presents an erythema in the regions exposed to the sun: the forehead, the cheeks, the bridge of the nose, the anterior part of the chest, the nape of the neck and the hands; this erythema appears in the spring and summer and disappears during the winter. The same cycle of exacerbations is observed with vernal conjunctivitis. In both diseases the exacerbations in the summer may be due to the presence during this season of the year of more intense sunlight, with a greater quantity of ultraviolet

1. Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, p. 404.

rays. These may help to destroy the riboflavin and the nicotinic acid or may create a greater demand for them by the organism, with production of the conjunctival erythema, in the case of vernal conjunctivitis, and the erythema of portions of the skin exposed to the sun's rays, in the case of pellagra.

Widmark demonstrated experimentally that the well known solar erythema is due not to the thermal, or visible, radiation, but to the ultraviolet rays, this erythema occurring more frequently during long climbs over snow-covered mountains. Under such conditions the ultraviolet rays, acting on the visual apparatus, may also give rise to the condition inadequately named "snow blindness." Electric (welders') ophthalmia, which in various degrees is produced by intense electric illumination, has the same cause. In cases of the mild form the process may give place to small alterations of chronic nature. Fuchs[2] mentioned the cases of persons "who, working under ordinary artificial light, felt no ocular disturbance whatever, but on being exposed to intense electric illumination were greatly troubled by a sensation of heat and itching of the eyes and by hyperemia of the conjunctiva and the palpebral margins." In the cases cited by Fuchs these symptoms, which are similar to those presented by vernal conjunctivitis, were probably caused by the ultraviolet rays of the electric illumination.

RIBOFLAVIN

On Jan. 14, 1933, Kuhn, Paul György, Wagner and von Jauregg identified vitamin B_2 in beer yeast. Then, after isolating the yellow pigment from skimmed milk, they prepared a crystallized derivate, which they called lactoflavin. In 1934 Kuhn and his collaborators succeeded in the total synthesis of vitamin B_2, their formula being $C_{17}H_{20}O_6N_4$. The substance exists in the form of yellow crystals, which are soluble in ethyl alcohol, water and acetic acid. It is more resistant than vitamin B_1 to dry and damp heat, remaining unchanged in the autoclave at a temperature 120 C.; it is also resistant to acids, but it is sensitive to alkalis and is easily decomposed by light and transformed to lumiflavin.[3]

Sherman, Bourquin and Euler fed rats artificial diets containing all the vitamins except riboflavin, and it has been proved that under these conditions, in order to obtain a gain in weight of 40 Gm. a month, it is necessary to feed each rat daily from 8 to 10 micrograms of riboflavin. This unit is known as a physiologic, or Sherman-Bourquin, unit and is at present the unit most widely used for the titration of this vitamin.

The lack of riboflavin, or ariboflavinosis (the better term would be hyporiboflavinosis), has been well described by Sydenstricker,[4] who stated that the ocular manifestations are of great importance and interest, as they furnish an easy method of identification of this deficiency before other symptoms appear. The ocular symptoms, which appeared at one time or another in 90 per cent of the cases studied by him, consisted of photophobia, burning and itching of the eyes, ocular fatigue, difficulty in far vision and amblyopia in semidarkness. For several years it has been known that amblyopia and cataract can be produced in rats by a diet deficient in riboflavin. It may well be said that the first symptom of ariboflavinosis is mild circumcorneal congestion, easily visible with the help of a lens. In cases of this condition notable proliferation and congestion of the limbic plexus can be detected with the slit lamp, and many new capillaries form a more or less complete arcade, which does not pass the borders of the cornea. As the avitaminosis progresses, severe interstitial keratitis develops, with predominating anterior vascularization. Other symptoms are cheilosis and erosion of the commissures of the lips (sebaceous dermatitis), the nasoliabial folds, the nasal wings and sometimes the ears and eyelids; the secretion of the sebaceous glands of the face seems altered, as blackheads may develop easily on the forehead, nose and chin; the tongue is clear, and the papillae are flattened rather than atrophic and are magenta red, the color differing from the scarlet characteristic of nicotinic acid deficiency.

The thiamine, the nicotinic acid and the riboflavin are essential factors in the intermediate metabolism of the carbohydrates, and when any of these three vitamins is lacking a complex disturbance in carbohydrate metabolism develops.

It is believed that the deficiency of riboflavin interferes with the mechanism of oxidation in the tissues; the excessive vascularization therefore may well be the answer of the tissues to a mechanism of deficient oxidation. Although little is known of the pathologic changes associated with this deficiency, it is believed that the lesions of the skin and of the mucosa may be due to local disturbances of cellular nutrition and of respiration, and that the changes in the eyes result from local cellular anoxemia. Probably the normal respiration of the vascular corneal tissues depends on the oxygen which the riboflavin can

2. Fuchs, E.: Tratado de oftalmologia, Barcelona, Editorial Labor S.A., 1936, p. 17.

3. Glandes endocrines et nutrition, in Laffont, A., and Durieux, F.: Encyclopédie médico-chirurgicale, ed. 10, Paris, 1939, pt. 10541, p. 10.

4. Sydenstricker, V. P.: Am. J. Pub. Health **31:** 344, 1941.

carry from the epithelium to the deep layers of the cornea; the lack of an adequate reserve of this vitamin in the cells of the cornea results in anoxemia, and the capillaries invade the tissue in order to carry the oxygen directly to the erythrocytes (Sydenstricker).

TREATMENT OF VERNAL CONJUNCTIVITIS

To date, therapeutics of vernal conjunctivitis has consisted principally of symptomatic treatment with an anesthetic to produce temporary relief from the inconvenience inherent in this disease. In addition, many kinds of treatment have been proposed: for example, the application of such astringents as zinc sulfate, boric acid and ichthyol; massage with mercuric oxide, and intravenous injections of calcium gluconate and a mixture of calcium chloride and urea (afenil). Radium therapy has been reserved for the more advanced stages, and then should be employed only in the hands of a specialist.[5] A change of climate, sea baths and cold showers used to be recommended, as well as a multitude of other measures, which in the majority of cases did not give satisfactory results.

The treatment which I have prescribed for my patients for the last two years consists in administration during the hot season of the year of from 1 to 3 tablets of riboflavin (1 mg. each, containing 400 Sherman units). As symptomatic therapy I prescribe a few drops of a solution of 0.05 Gm. of tetracaine hydrochloride and 15 drops of epinephrine hydrochloride (1:1,000) in 5 cc. of distilled water, the solution to be used only when the symptoms become accentuated. I advise the patient, in addition, to drink the greatest possible amount of milk, because milk is rich in riboflavin, containing 90 per cent of the vitamin in free form. With the treatment described, 35 patients, or 35.7 per cent of those treated, showed improvement in all ocular symptoms on the third or fourth day; 62 patients, or 65.1 per cent, showed improvement in from ten to fifteen days; the rest, 9 patients, did not return for examination.

Despite the improvement, in view of the chronicity of the disease, it is necessary to continue administration of the riboflavin in smaller doses, at least during the summer, when the symptoms appear. The following year it is advisable to begin the treatment before the warm weather begins, to prevent recurrence of the symptoms. As I said before, because this disease is one of many years' duration, it is not yet possible to draw definite conclusions; however, on the basis of the results thus far obtained with the treatment described, ariboflavinosis is to be considered as the possible cause of vernal conjunctivitis.

CONCLUSIONS

Clinically ariboflavinosis presents certain definite symptoms, with ocular manifestations similar to those occurring in vernal conjunctivitis.

Widmark demonstrated experimentally that solar erythema is due to exposure to ultraviolet rays, and it is generally accepted that the same rays produce so-called *snow blindness* and electrical ophthalmia.

The good results obtained thus far with riboflavin in the *treatment* of vernal conjunctivitis lead one to believe that ariboflavinosis may be the cause of this disease.

Aldama 112.

5. Gifford, S. R.: A Hand-Book of Ocular Therapeutics, ed. 3, Philadelphia, Lea & Febiger, 1942, pp. 238-240.

A PRACTICAL OPHTHALMIC TEST WHICH FURNISHES QUANTITATIVE DATA

MODIFICATION OF THE MASSACHUSETTS VISION TEST

ALBERT E. SLOANE, M.D.
Director, Department of Refraction, Massachusetts Eye and Ear Infirmary
BOSTON
AND
J. ROSWELL GALLAGHER, M.D.
School Physician, Phillips Academy
ANDOVER, MASS.

In another report [1] the results of examination of the eyes of 1,009 adolescents were described, and the number found, by each of a series of tests, to have visual defects was discussed. The testing of vision as part of an annual medical examination of adolescents is an important procedure and in the ideal situation would most effectively be carried out by a qualified ophthalmologist. Since such highly qualified members of the personnel are seldom available, one must usually rely on a screening device designed to select persons who would benefit by a more thorough examination. For such purposes the Massachusetts vision test [2] has proved adequate; this test has recently been approved by the National Committee on Optics and Visual Physiology and by the Council on Physical Therapy of the American Medical Association.[3]

However, there is a need, under certain conditions, for a visual test which furnishes quantitative data for purposes of classification and yet can effectively be administered by a technician. Such a battery of tests could presumably be employed to grade persons as to their ocular capacity, after vision had been corrected as far as possible by the ophthalmologist and might serve as an aid in determination of visual eligibility for various tasks and in the assignment of industrial personnel to different occupations and services. Such tests would also make available comparable data for certain research problems; in one group it has already been of aid in estimating eligibility for the various branches of the armed forces. As a result of two years' experience with the group already referred to,[1] as well as the experience of one of us (A.E.S.) with the Massachusetts vision test, such a test has been developed. This method is a modification of the Massachusetts vision test; changes in that test have been made so that quantitative data will be available for special situations demanding them; it does not replace the Massachusetts vision test as a method of screening out school children. In the present report this modification is described; our experience with it in testing 797 adolescents is discussed and its efficiency is evaluated.

METHOD

All students attending the regular session and a summer session at a boys' preparatory school were tested; these 797 boys ranged from 12 to 19 years of age. A technician who had a brief period of instruction (two hours of training is sufficient) from one of us (A. E. S.) carried out the testing of 707 boys in September, and a similarly trained technician tested 90 other boys in July. The equipment consisted of a well illuminated testing board measuring 36 by 48 inches (91 by 122 cm.); the board was of plywood and was painted a dull black; gummed numbers and letters 1 inch (2.5 cm.) high were spaced 6 cm. apart to form a Maddox cross so that the value of each unit at the testing distance (20 feet [6 meters]) equaled 1 prism diopter (fig. 1). At the exact center of the board a hole, ½ inch (1.27 cm.) in diameter, permitted light from a 5 watt, nonfrosted bulb to be seen—the bulb was mounted in a receptacle attached to the back of the board. A Snellen test chart, approved by the American Medical Association, was divided in half, and one-half was placed in each upper quarter of the board. The center light and the lights illuminating the board were controlled by an extension switch located conveniently for the technician. The illumination on the test chart averaged 20 foot candles. Four pairs of spectacles were used. In one pair two + 1.50 D. spheres were mounted; another pair contained a red multiple Maddox rod mounted horizontally for the right eye and no lens for the left eye, and another, a red multiple Maddox rod mounted vertically for the right eye and no lens for the left eye. The Maddox rods and plus spheres were the same as

From the Department of Health, Phillips Academy.

This study was aided by a grant from the Carnegie Corporation.

1. Sloane, A. E., and Gallagher, J. R.: A Summary of Findings at the Eye Examination of Preparatory-School Boys, Am. J. Ophth. **26**:1076 (Oct.) 1943.

2. Sloane, A. E.: Massachusetts Vision Test, Arch. Ophth. **24**:924 (Nov.) 1940.

3. Massachusetts Vision Test Acceptable, report of the Council on Physical Therapy, J. A. M. A. **122**:37 (May 1) 1943.

those used in the Massachusetts vision test. In the fourth pair two 3 D. prisms were mounted base up for the right eye and base down for the left eye. A card (fig. 2) calibrated so that each letter and number equaled 1 prism diopter at 16 inches (19.8 cm.) was used for the phoria test for near vision.

The subject was seated 20 feet (6 meters) from the test board; the technician was seated at the subject's right and facing him. First, visual acuity for each eye and then for both eyes, without glasses, was tested and recorded; next, with glasses, if they were worn, vision for each eye and for both eyes was determined. Vision for each eye and for both eyes with the + 1.50 D. spheres was tested and was recorded if vision was 20/40 or better. This test was made with glasses, if they were worn. Measurements of heterophoria were recorded by the letter or number through which the red streak produced by the Maddox rod spectacles appeared to pass: The use of these letters and numbers obviated any confusion as to whether the streak passed to the right or to the left of the center, or above or below it. Heterophoria for near vision was measured by recording the letter or number under which the second arrow apparently was placed; the card (fig. 2) and the prismatic lenses were used in this test. Questions regarding the date of the last thorough ophthalmic examination and whether or not glasses were worn constantly were asked by the technician, and the answers were recorded. The entire examination by the technician did not require more than four minutes.

At the point in his health examination at which the student was examined by the school physician (J. R. G.) he was asked regarding headache, blurred vision and eyestrain, and the technician's notes were reviewed and evaluated. At that time each student's record was marked "pass," "refer" or "refer S," the last category including all borderline cases and signifying that a more thorough examination was indicated if any symptoms of eyestrain should develop. The records of all students who had symptoms suggesting "eyestrain," regardless of the results of any of the tests, were marked "refer," as well as the records of all students with less than 20/30 vision in either eye, all students with more than 4 prism diopters of exophoria, 6 prism diopters of esophoria or 1 prism diopter of hyperphoria for distance; all students with 6 prism diopters of esophoria or 8 prism diopters of exophoria for near vision, and all students with 20/20 vision in either or in both eyes with the + 1.50 D. spheres.

Fifty-five students, the majority of whom were members of this group of 797 boys, and all of whom had had similar screening tests, were subsequently carefully examined by one of us (A. E. S.). The results obtained at the office visit were compared with those recorded at the time of the screening tests, in an effort to evaluate the efficiency of these brief and simple screening procedures.

RESULTS

Visual Acuity.—Seven hundred and ninety-seven boys were tested. Of these, 518 boys (65 per cent) did not wear glasses; of the latter number, 16 had 20/30 vision in one eye, 1 had 20/30 vision in both eyes and 11 had 20/40 vision or less in one eye or in both eyes. Two hundred and seventy-nine boys (35 per cent) had glasses; when these boys were tested without their glasses, 13 had 20/30 vision in one eye, 5 had 20/30 vision in both eyes and 161 had 20/40 vision or less in one eye or in both eyes; the others had 20/20 vision. When tested with their glasses, 15 of the 279 boys had 20/30 vision in one eye. 8 had 20/30 vision in both eyes and 39 had

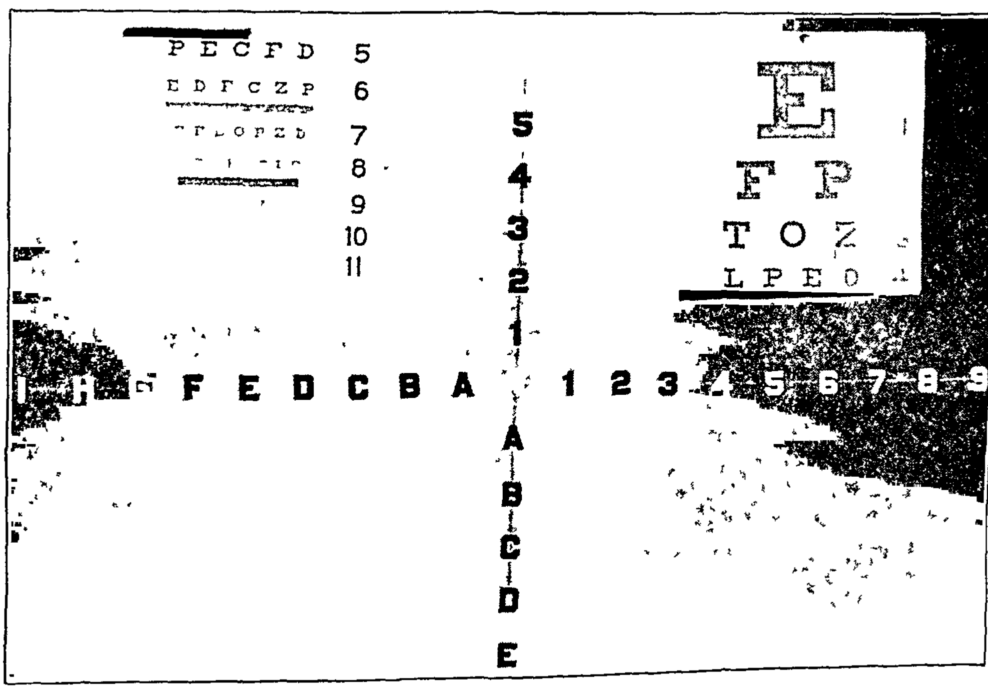

Fig. 1.—The testing board used in the modified test.

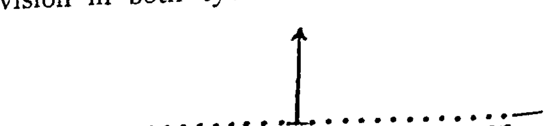

Fig. 2.—Card used to test heterophoria for near vision (A. E. Sloane), calibrated for a distance of 16 inches.

20/40 vision or less in one eye or in both eyes; 16 of these boys had not consulted their ophthalmologist within the previous twelve months, and their records were therefore marked "refer"; the others were considered to have deliberately been given less than full correction. Table 1 summarizes these data.

TABLE 1.—*Summary of Observations in the Part of the Modified Massachusetts Vision Test Designed to Measure Visual Acuity*

Number of students tested	797
No. of students who had glasses	279 (35%)
No. of students who without their glasses had 20/20 vision	100
No. of students who without their glasses had 20/30 vision in one eye or in both eyes	18
No. of students who without their glasses had 20/40 vision or less in one eye or in both eyes	161
No. of students who with their glasses had 20/20 vision	217
No. of students who with their glasses had 20/30 vision in one eye or in both eyes	23
No. of students who with their glasses had 20/40 vision or less in one eye or in both eyes	39
No. of students who did not have glasses	518 (65%)
No. of students who had 20/20 vision	490
No. of students who had 20/30 vision in one eye or in both eyes	17
No. of students who had 20/40 vision or less in one eye or in both eyes	11

Hypermetropia.—Four of the 279 boys who wore glasses had 20/20 vision with their glasses and the + 1.50 D spheres. Thirty-six (6.9 per cent) of the 518 boys who did not have glasses had 20/20 vision with the + 1.50 D. spheres. Only 1 of these 40 boys would have been graded as "referred" on the basis of his visual acuity test.

Heterophoria. — Heterophoria (Distance): Twenty-five boys (3.1 per cent) had more than 4 prism diopters of exophoria or more than 6 prism diopters of esophoria for distance. One of these 25 students failed with the visual acuity test, and 3 failed with the test for hypermetropia.

Hyperphoria (Distance): Twelve boys (1.5 cent) had more than 1 prism diopter of hyperphoria. Two of these failed with the visual acuity test, and 4 others failed with the horizontal phoria test.

Heterophoria (Near Vision): Twenty boys (2.5 per cent) had more than 6 prism diopters of esophoria or more than 8 prism diopters of exophoria for near vision. Eleven of these students failed with the distance heterophoria test and 4 others failed with the visual acuity test.

Symptoms.—One student who gave satisfactory results with all tests was referred to an ophthalmologist because of "blurred vision"; no other student with this complaint passed all the tests. Two boys who gave satisfactory results with the tests were referred because of "headache"; no other student with headache passed all the tests. The manner in which these questions are asked and the answers interpreted is obviously an important factor.

Referral.—On the basis of the results in the visual acuity test alone, after exclusion of subjects with glasses who had been examined by their ophthalmologist within twelve months, 44 students with vision of 20/30 or less (with glasses if glasses were worn) in either eye would have been referred to an ophthalmologist. If the standard for passing had been lowered to vision of 20/30 or less in both eyes, 24 students would have been referred on the basis of the visual acuity test alone, and if the standard had been lowered to vision of 20/40 or less in either eye, 21 boys would have been referred. Of the 518 boys who did not have glasses, 16 had vision of 20/30 in one eye, 1 had vision of 20/30 in both eyes and 11 had vision of 20/40 or less in one eye or in both eyes. The large percentage of students who already had glasses decreased considerably the number referred on the basis of the visual acuity test; 161 boys (20.2 per cent of the entire group) whose visual acuity without glasses was 20/40 or less already had glasses. Students who had glasses and who had seen their ophthalmologist within the previous twelve months were not referred, even if the our findings were abnormal, but their specialist was advised of the results of our examination and the subsequent recommendation left to his judgment.

Ability to read the 20/20 line through a + 1.50 D. sphere is generally accepted as an indication for a careful examination by an ophthalmologist. Thirty-nine of the 40 boys who failed the plus sphere test passed the visual acuity test; none had vision of less than 20/30 in one eye, and only 5 of the 39 boys failed in any part of the heterophoria tests. The fact that 100 of the 279 boys who wore glasses had vision of 20/20 suggests that a considerable percentage of the entire group with hypermetropia had already had this condition corrected.

TABLE 2.—*Summary of Results with Portions of the Modified Massachusetts Vision Test for Measurement of Hypermetropia and Heterophoria*

Total number tested	797
No. of students who had glasses	279
No. who had 20/20 vision with their glasses and +1.50 D. spheres	4
No. of students who did not have glasses	518
No. who had 20/20 vision with +1.50 D. spheres	36
No. of students who failed with test for heterophoria (distance)	25
No. who failed with this test but passed all others	21
No. who failed with the test for hyperphoria (distance)	12
No. who failed with this test but passed all other tests	6
No. who failed with the test for heterophoria (near vision)	20
No. who failed with this test but passed all other tests	5

The number of additional patients selected for referral through failure with the tests for heterophoria was not large, but the small percentage of such boys who also failed with other tests is significant. Only 4 of the 25 boys who failed with the horizontal (distance) phoria test failed with either the visual acuity test (i. e., had vision of less than 20/30 in one eye) or the hypermetropia (plus sphere) test. On the basis of these three tests for heterophoria, 32 boys who were not selected by other tests were referred to an ophthalmologist. Of the 518 boys who did not have glasses, 25 failed with at least one of the heterophoria tests and did not fail with either the visual acuity or the plus sphere test.

Summary.—Twenty-eight students, about 5 per cent of those who had no glasses, had vision of 20/30 or less in one eye or in both eyes. Sixteen students who had glasses had vision of 20/30 or less in one eye or in both eyes and had not been examined by an ophthalmologist within the previous twelve months. Forty other boys, or 5 per cent of the entire group, 36 of whom did not have glasses, had 20/20 vision with + 1.50 D. spheres in either eye or in both eyes. Thirty-two more students, or 4 per cent of the entire group, failed to meet the standards set for the tests for heterophoria. In all, a total of 116 boys, or about 14 per cent of the entire group, were considered to be in need of a more thorough examination in the near future. Of the 518 boys who did not have glasses, 17 per cent were referred to an ophthalmologist. Others, whose vision was not quite normal but for whom tests showed vision within the standards set, were instructed to seek advice if symptoms of eyestrain developed.

COMPARISON OF RESULTS OF THE SCREENING TEST AND OF THE SPECIALIST'S EXAMINATION

Fifty-five students who on the basis of the screening test were referred to an ophthalmologist for a more thorough examination of the eyes were seen by one of us (A.E.S.), and an estimate of the efficiency of the screening test was possible by a study of the observations at that examination and at the subsequent one, made by the specialist.

Nineteen of the 55 students were referred because of failure with the visual acuity test, and in no instance did the specialist find that the referral was unnecessary. Fourteen students were referred on the basis of failure with the plus sphere test: For 3 of these no accessory treatment was indicated because no symptoms were present and there was adequate amplitude of accommodation for compensation; the other 11 boys required treatment. Eight students were referred because of failure with one or more of the tests for heterophoria: 2 of these boys required no treatment because of absence of symptoms and the presence of adequate compensation through a large amplitude of fusion. During the course of the year, 14 other students were referred solely on the basis of symptoms suggesting eyestrain; 5 of these boys needed no treatment.

Ten of the 55 students referred to the specialist were found not to need any treatment; 5 of these were referred because of symptoms alone, and the other 5 were observed to have the abnormality noted at the screening examination, but sufficient amplitude of fusion or accommodation for adequate compensation was present. It is obvious that referral on the basis of symptoms alone is often unnecessary; difficulty in assessment of symptoms is responsible for this error.

In 4 of the 55 boys examined by the specialist conditions which had not been detected by the screening examination were observed. Three had a sufficient amount of heterophoria to produce symptoms due to a low amplitude of fusion; for each patient the degree of heterophoria was within the limits set for the screening test and therefore had not been considered significant at the time of that examination. The other patient, who had been referred on the basis of symptoms alone, was found to have latent hypermetropia; yet he had passed the plus sphere test.

The results of the screening test and the specialist's examination for the 55 students who were referred to an ophthalmologist are summarized.

No. who failed with modified Massachusetts vision test for visual acuity	19
No. who failed at specialist's examination	19
No. who failed with plus sphere test at modified Massachusetts vision test	14
No. who failed with this test at specialist's examination	14
(Of these, 3 patients were asymptomatic and had adequate compensation; so no treatment was required.)	
No. who failed with modified Massachusetts vision tests for heterophoria	8
No. who failed with those tests at specialist's examination	8
(Of these, 2 patients required no treatment because they had adequate compensation and were asymptomatic.)	
No. who were referred on basis of symptoms, but did not fail with any other part of modified Massachusetts vision test	14
No. found by the specialists to require treatment	9

COMMENT

The Massachusetts vision test is a valuable and satisfactory method of screening out school children who require the attention of an ophthalmologist. This test is divided into three parts:

first, a test for visual acuity; next, a test for the detection of latent hypermetropia of a substantial degree, and, last, a test of binocular balance. No attempt is made to evaluate the visual error or the particular reason that a child is referred for a more complete ophthalmic examination, and when failure occurs in any one test the remaining tests are omitted.

In the modification of the Massachusetts vision test described here the following changes have been made. In part I visual acuity both with and without glasses is determined, and in part 2 the plus sphere test is given, both with and without glasses if glasses are worn. All parts of the test are given even though failure of one part constitutes sufficient reason for referral. Part 3, which is the test for the presence of heterophoria, has been modified. With the Massachusetts vision test the dimensions of the window and house set the limits for passing or failing in the test, and no specific quantitative estimations of the degree of heterophoria can be made. This is deliberate, since the aim of the test is not to act as an aid in diagnosis, but rather to serve as an indicator for referral of persons in need of further ocular examination. The modification we have employed calls for the use of a tangent scale calibrated in prism diopters (Maddox cross) so that direct quantitative readings can be made. In a similar way, in the heterophoria test for near vision, which utilizes the dimensions of the face of a testing object as the limit for passing the test, there has been substituted a tangent scale calibrated in prism diopters. The features of the Maddox rod have been retained for the distance heterophoria test, but fusion has been broken by the introduction of appropriate displacing prisms to make possible the heterophoria test for near vision. These changes have made it possible to obtain quantitative data for each part of the test and to modify at will the limits for passing or failing without alteration of the test unit. For the strict purpose of screening out from a group of children those who should be referred to an ophthalmologist for a more thorough examination, quantitative readings or utilization of subsequent tests is unnecessary after the child has failed with one test, and therefore referral is inevitable.

This modification of the Massachusetts vision test has increased to a slight extent the time necessary to examine each subject, but the number of minutes for each test is still small. Intelligent subjects can easily be tested in less than four minutes: It is obviously important to utilize a technic which not only is reliable but can be administered with reasonable rapidity. It is also important that the technics of the test be simple enough so that persons with little training can administer them accurately. Our technicians, who had not more than two hours' training, were able to carry out the tests efficiently.

The number of children in this group found to require a more thorough examination was not large, but the small proportion was undoubtedly due to the group's being a highly selected one from the economic standpoint. Children from lower family income groups probably would have a higher percentage of visual defects which had not previously been corrected. However, the discovery that about 18 per cent of children who did not have glasses required a more thorough examination indicates the value of this sort of test even for adolescents whose economic background is favorable. It is undoubtedly an essential part of the annual health examination of members of such a group.

The validity of these screening devices can be tested by a comparison of the results obtained with these tests and the observations of the ophthalmologist. Agreement between the estimates of visual acuity made at each of these two examinations was excellent, and in no instance in which a student was referred did the specialist find that he had normal vision. Some of the students who were referred to a specialist because of failure with the plus sphere, or heterophoria, test were found to have adequate compensation for their abnormality, and therefore not to be in need of treatment, but in every instance the condition discovered by the screening test was also observed by the specialist. A screening test, however, cannot detect all abnormalities and cannot distinguish between conditions for which compensation is and those for which it is not adequate. In a small number of the students referred to the specialist, he observed conditions of significance which had not been considered important at the screening examination because the results were within the limits of normal agreed on. It is probably inevitable that a few persons with low errors but concomitant low compensatory factors will be overlooked by any screening examination.

SUMMARY AND CONCLUSIONS

A modification of the Massachusetts vision test makes it effective for the obtaining of quantitative data.

This technic differs from the Massachusetts vision test in that it provides quantitative measurements of heterophoria and calls for a report on all parts of the test, although the subject may have failed with one part and therefore referral is inevitable.

This screening examination has the same objectives as the Massachusetts vision test, of which it is a modification, namely: (*a*) brevity, so that large numbers of subjects may be examined in a brief period; (*b*) simplicity of technic, so that the test may be administered by lay persons after very brief training; (*c*) detection of latent errors of hypermetropia and binocularity, as well as of visual acuity; (*d*) simplicity and inexpensiveness of equipment, and (*e*) efficiency in selection of persons who require a more complete examination by an ophthalmologist.

About 14 per cent of the members of an economically privileged group of adolescents were found to require a more thorough examination by an ophthalmologist. About 5 per cent were referred on the basis of the plus sphere test and about 4 per cent because of failure with a test for heterophoria: These results indicate the desirability of such tests, as well as of a test for visual acuity. About 5 per cent failed with the visual acuity test.

Results with the screening examination were in close agreement with the observations made at a subsequent examination by an ophthalmologist.

With this modification of the Massachusetts vision test quantitative measurements of heterophoria are obtained for distance and for near vision; this permits change in the limits for passing the test at any time without alteration in method or equipment.

This modification of the Massachusetts vision test does not replace the Massachusetts vision test in its sphere of usefulness as a means of screening out children who require further examination of the eyes; the test described has application only when quantitative visual data are required.

The modified test may be employed to grade persons as to their ocular capacity and may be useful in selection of personnel.

416 Marlborough Street, Boston.

Isham Infirmary, Andover, Mass.

OCULAR MALINGERING

CAPTAIN HOWARD AGATSTON

MEDICAL CORPS, ARMY OF THE UNITED STATES

Recent reviews describing the various tests for malingering have appeared in the literature.[1] It is not my purpose to duplicate this work; rather, I wish to present the following material:

1. A workable classification of ocular malingering in which the more useful special tests are placed where they can be used to greatest advantage.

2. A correlation table to serve as a guide to the ophthalmologist in evaluating exaggeration of poor uncorrected vision.

3. A statistical analysis of the true monocular amblyopias to show the wide range of corrected vision.

4. A quantitative test for binocular stereopsis [2] for use in detection of simulated monocular amblyopia.

OCULAR MALINGERING

Incidence in Army Induction Examinations.—Fortunately, the incidence of ocular malingering in routine Army induction examinations is low. Although no accurate statistics are available, it is safe to put the figure between 0.5 and 3 per cent. This seems negligible, but it means that of every 1,000,000 men examined, 5,000 to 30,000 are ocular malingerers.

Definition.—Malingering may be defined as the false assertion, exaggeration or denial, either by history or by performance, of the existence or origin of a physical defect.

Positive malingering includes simulation, false attribution and exaggeration. Shastid [3] gave the following definitions:

> Simulation is the feigning of an ocular disease or injury which does not exist. False attribution is the assignment of an untrue cause to an existent disease or injury. Exaggeration is the pretense that an injury or disease which really exists is greater in extent or severity than is really the case.

Negative malingering is denial or dissimulation of an existent disease or defect.

The Malingerer.—The positive malingerer has one of the following aims: (1) to evade all military service; (2) to obtain a limited, or perhaps a noncombatant, status, or (3) to obtain discharge from the army with or without compensation.

Some malingerers are naive and easily discovered, while others, shrewd and practiced, are exposed only after numerous tests. The positive malingerer dreads a leisurely and searching examination and, as time wears on, becomes increasingly nervous and tense. Occasionally a candidate assumes a patriotic "please take me in" attitude in order to conceal his real intention and mislead the examiner. Then there is the man who with some reluctance, but with obvious relief, suddenly decides to be truthful when threatened with detection, and covers his earlier responses with lame excuses.

The negative malingerer is exemplified by the young volunteer who by squinting, peeking, tilting the head or memorizing the chart hopes to obtain sufficient vision for acceptance. Older men, eager for service, also withhold knowledge of a defect and tend to minimize their failures.

The Examiner.—While in private practice the veracity of the patient is seldom questioned, in Army induction examinations the honesty of the candidate must frequently be proved.

The Army ophthalmologist should approach the patient in a friendly and sympathetic manner. Not only is the examiner under keen observation, he may even be questioned as to the degree of his training by the clever malingerer, who will vary his testimony accordingly. The examinee should be given ample time to tell his story, as his manner of telling it may be revealing.

The negative malingerer may be detected only after a careful and complete routine examination. The eye is inspected by direct and oblique illumination. The tactile tension is taken for all candidates over 38 and is checked if necessary by tonometry. Ocular motility, pupillary reactions, the media and the fundi are examined. Such an all-inclusive study will disclose disqualifying conditions, such as chronic simple glaucoma, chronic low grade uveitis and retinitis pigmentosa, despite normal central vision. Confron-

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From the General Dispensary, United States Army, New York.

1. Chase, S.: Eye Examination Complicated by Conscious Exaggeration, M. Bull. Vet. Admin. **17**:331 (April) 1941. Lasky, M.: Simulated Blindness, Arch. Ophth. **25**:1038 (June) 1941. Sugar, H. S.: Malingering in Ophthalmology, Dis. Eye, Ear, Nose & Throat **2**:42 (Feb.) 1942.

2. Verhoeff, F. H.: Simple Quantitative Test for Acuity and Reliability of Binocular Stereopsis, Arch. Ophth. **28**:1000 (Dec.) 1942.

3. Shastid, T. H., in Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, 1189.

tation tests and perimetric studies may be needed to rule out visual disturbances of central origin.

The positive malingerer is detected only after the routine examination is supplemented by special tests. Full use should be made of all available tests, and they should be applied so quickly and smoothly that within a few minutes even the practiced and clever malingerer is thrown into confusion and betrays himself. The incidence of recognized malingering varies with the thoroughness of the examiner.

Malingering and true disease may coexist, and in the zeal of discovering a cheater the examiner may overlook an associated disease. Furthermore, not all candidates suspected of malingering prove to be dishonest, and the possibility of erroneous accusation must be carefully avoided.

The examiner must not try to force an admission of malingering by intimidation, but he should be capable of demonstrating the existence of simulation. If malingering appears probable and yet is difficult to prove, the examiner is justified in resorting to suggestion; i. e., he may ask questions as to the existence of symptoms entirely alien to the disorder feigned. An abrupt question, such as "What's the matter with you?" or "I don't believe you," may surprise a malingerer into confession. Ridicule of the candidate's poor success in feigning a disease may also produce the desired effect. The examiner may appear to believe the malingerer's story and watch the effect of excessive display of sympathy. He may instil fear by hints of some drastic or disagreeable mode of treatment.[4]

Prolonged observation, direct and indirect, will evoke some inconsistency. The more protracted the examination, the more it irks the malingerer, who is hard put to avoid slips.

In doubtful cases a second examination is made one to several days later, perhaps by another qualified examiner. Meanwhile, affidavits from private ophthalmologists and hospitals are evaluated, and further details may be requested. Affidavits of ophthalmic examinations made just prior to induction into the Army are in some instances to be viewed with suspicion.

CLASSIFICATION OF OCULAR DEFECTS

To simplify detection of the malingerer, all the ocular defects that can be simulated are for convenience classified under four main heads: (1) errors of refraction; (2) the amblyopias; (3) organic disease, and (4) defects in color vision. Nearly all malingering, whether positive or negative, will fall under one of these four heads although various combinations are encountered.

I. ERRORS OF REFRACTION (UNCORRECTED VISION)

Positive Malingering.—The candidate with a refractive error, usually myopia or compound myopic astigmatism, reads perfectly with his own glasses, with or without further correction, but exaggerates his diminished uncorrected vision in the hope of evading military service altogether or of qualifying for some form of noncombatant duty. Keeping in mind the degree of uncorrected vision he admits, the examiner proceeds to make a brief retinoscopic study, preferably with an electric instrument and under dynamic conditions. Accommodation is for the most part eliminated by use of a fixation point at 20 feet (6 meters), such as the muscle light. Cycloplegia is impractical in mass examinations and is rarely necessary. The retinoscopic examination indicates with close approximation what correction is needed for 20/20 vision and what the vision without glasses should be. The correlation of various correcting lenses with the corresponding uncorrected vision is well known and is sufficiently exact to be recorded, as is done in table 1.

TABLE 1.—*Correlation of Uncorrected Vision with Refractive Error* *

Spheres, Diopters	Cylinders, Diopters								
	0	—0.50	—1.00	—1.50	—2.00	—2.50	—3.00	—3.50	—4.00
0	20	25	30	50	70	100	200	300	400
—0.50	30	30	40	60	80	100	200	300	400
—1.00	50	50	60	70	100	150	250	350	400
—1.50	70	70	80	100	150	200	300	400	
—2.00	100	100	150†	200	250	300	400		
—2.50	200	200	250†	300	350	400			
—3.00	300	300	350†	400	400				
—3.50	400	400	400						

* The figures are the denominators of the visual acuity, the numerator in each case being 20.
† 20/150 is equivalent to 13/100; 20/250, to 16/200, and 20/350, to 17/300.

Table 1 gives the values for myopia, myopic astigmatism and compound myopic astigmatism and is based on the results of experiments with 6 Army men. These subjects, each with less than 1 D. of refractive error, had full correction, and, one eye being used at a time, the various refractive states were simulated by employment of plus lenses at the anterior focal plane. For example, the vision of an eye with compound myopic astigmatism requiring a correction of — 100 D. sph. ⊃ — 0.50 D. cyl., axis 180 was obtained by placing a + 1.00 D. sph. and a + 0.50 D. cyl., axis 180 in the trial frame. Latent hyperopia and spasm of accommodation when present were neutralized prior to the experiment by adequate fogging. In this way cycloplegia, with its attendant mydriasis, was

4. Beaumont, W. M.: Malingering in Relation to the Eye, in Jones, A. B.: Malingering or the Simulation of Disease, Philadelphia, P. Blakiston's Son & Co., 1918, chap. 19, pp. 324-415.

avoided. It was found that the need of a cylinder axis 90 or axis 180 made little or no difference in the vision. In order not to complicate the table, vision of eyes requiring oblique axis cylinders was not recorded, but it was found that when the cylinder was more than 15 degrees off either of the main axes, the subject read one or two lines less if the error of refraction was 1 D. or more. The figures in this table are in close agreement with actual values for honest candidates. They are average values, and the table serves only as a guide.

A similar correlation chart could be made for hyperopia, hyperopic astigmatism and compound hyperopic astigmatism, as well as for mixed astigmatism, but there would be little occasion to refer to them, since candidates with these errors almost invariably have 20/100 vision or better. If necessary, the examiner, using himself as a subject, may properly simulate any refractive error he may encounter. Amplitude of accommodation and the presence and degree of presbyopia must be kept in mind. Thus, a man 35 years of age with hyperopia of 6 D. should normally be able to overcome 4 to 5 D. by accommodation, and the uncorrected vision will be equivalent to that of a man with myopia of 1 to 2 D.

Admittedly, there are borderline cases, and it is in these that the subjective element must be taken into consideration. The malingerer does not have the "will to read" and refuses to recognize any letters that appear the least bit blurred. If he is not clever in his deception, he will read much less than is expected from the correlation chart, and the discrepancy will prove his dishonesty. In the honest candidate with borderline uncorrected vision the "will to read" is apparent. His visual acuity may of course improve with rest, fogging and the elimination of glare. The malingerer may feign a desire to cooperate by asking if he can squint, or he may obviously oversquint and then further disappoint the examiner by reading much less than one would expect as a result of squinting.

When the uncorrected vision is insufficient for full service, reliance cannot be placed on the subject's own glasses, and retinoscopic examination is indicated. This will expose the man innocent of a slight overcorrection, as well as the bold emmetrope who wears — 5.00 D. spheres in an attempt to simulate myopia. The latter, because of youthful accommodation, is able to read 20/20 through these thick concave lenses.

Although retinoscopic examination is imperative in the detection of simulation or exaggeration of a refractive error, several supplementary procedures may be used.

Vision at 10 and 5 feet (3 and 1.5 meters) should be consistent with that at 20 feet (6 meters). At the shorter distances slight allowance must be made in the case of the myope. As the chart approaches his far point and his eye remains unaccommodated, his vision is better than the mathematical expectation; e. g., if his vision is 20/400, it will be 10/200 + and 5/70. By means of the mirror test (mirror and reverse chart) vision at 40 feet (11.5 meters) may be taken. By his being made to look through a tube 1 meter long, the malingerer is ignorant of his distance from the chart, and the vision obtained at different distances may be inconsistent.

The naive malinger who is willing to read the third line from the top can sometimes be fooled if one projects the 20/70 line as the top one.

Near vision should correspond with the refractive error. A man with a myopia of — 4.00 D. will read Jaeger type 4 at 14 inches (36 cm.), whereas one with myopia type of — 3.00 D. will read Jaeger type 1. A subject with astigmatism of — 2.00 D. will read Jaeger type 2 or 3, whereas one with astigmatism of — 1.00 D. will read Jaeger type 1 or 2.

Binocular tests, as described under "The Amblyopias," are applicable here when the subject claims an appreciable difference in the uncorrected vision of the two eyes.

Negative Malingering.—Negative malingering of uncorrected vision is practiced by candidates who are eager for service. While determining the visual acuity the examiner makes certain that each eye, in turn, is properly occluded. The head is held straight, and the exposed eye is not squinted. Routinely the left eye is covered first. This, together with close scrutiny, will help to expose the man with good vision in only one eye who, when told to cover his other eye, merely places the occluder in the other hand and then covers the same eye. The projector should be adjusted in advance so that the examiner does not have to look away from the subject. Malingering by memorization is controlled by the examiner's changing the charts or slides. In suspected cases dynamic retinoscopy is indicated.

In the hope of temporary improvement in vision, miotic drugs are sometimes resorted to. If the examiner's suspicion is excited, examination should be postponed, or, after the usual precautions, a mydriatic can be given, and, if there is no appreciable spasm of accommodation, the vision can be determined after the miosis is overcome.

II. THE AMBLYOPIAS

Positive Malingering.—By amblyopia is meant subnormal vision (less than 20/30 with the best possible corrective lenses) which is unaccounted

for by detectable organic changes in the external eye, fundus, optic pathways or brain centers.

1. Simulated Binocular Amblyopia: I was able to find only 11 bona fide instances of binocular amblyopia among 20,000 cases. One was that of a man whose vision was corrected to 20/40 in the right eye with + 4.00 D. sph. ⊃ + 2.75 D. cyl., axis 110 and to 20/50 in the left eye with + 3.00 D. sph. ⊃ + 2.75 D. cyl., axis 90. The eyes were straight. My observations were checked by a reliable affidavit of an examination done a number of years ago. The subject's poise and attitude after prolonged examination gave further corroboration of the results. Seven of the patients had congenital nystagmus. Four of these men also had high myopia, and 2, high mixed astigmatism. One patient was an albino. Corrected vision varied from 20/40 to 20/200.

In contrast, I found simulated binocular amblyopia somewhat more common.

1. The history should include data on heredity, disease and trauma. The records of previous examinations, both civilian and military, should be obtained for comparison. One must decide whether the past and the present vocations conform to the limitation in vision.

2. The examination should rule out organic disease. At this point retinoscopic examination and refraction are carried out; the corrective lenses are placed in the trial frame, and one eye is occluded. The naive malingerer may read down on the Snellen chart if a weak minus sphere is added or if a stronger sphere or cylinder is used and then neutralized. Or one may apply the Hesse test. This consists of fogging the eye with a + 3.00 D. or a + 4.00 D. lens and then gradually reducing the strength 0.5 D. at a time in the hope that when the original prescription is reached an extra line or two will be read.

3. The visual angle is changed as described under "Errors of Refraction." Near vision should be determined and its correspondence to distant vision evaluated. Some examinees who refuse to see the smaller Jaeger test types do not hesitate to read numbers on the ophthalmoscope dial.

4. Provocative statements, vitriolic or facetious, may be typewritten or printed for the selectee to read. The reaction of the malingerer may be revealing.

5. Using the element of surprise, the examiner nonchalantly drops a pin, coin or clip, and the unthinking subject who is simulating amblyopia unconsciously recovers it. He is suddenly asked to fix on some small object for a screen cover test; orthophoria is demonstrated, and, furthermore, the subject does not complain of the small size of the fixation object.

6. Examination of the handwriting of the candidate, e. g., on application blanks or laboratory slips, may be enlightening. Without his knowledge, the man should be observed for clues to the acuity of his vision by as many members of the personnel as possible. For example, one suspect was seen reading the newspaper at a distance of about 5 inches (13 cm.) and a few minutes later anxiously perusing his physical examination sheet at a distance of 12 inches (30 cm.).

Tests for monocular amblyopia are applied if good vision has been proved to exist in one eye.

2. Simulated Total Blindness in One or Both Eyes: The history and results of examination will rule out organic disease. Particular attention should be paid to the pupillary reactions. Beaumont [4] summed up this subject as follows:

> When a bright light is flashed into the eye, two noticeable reflexes occur, first a contraction of the pupils and, secondly, a spasmodic closure of the lids from the dazzling effect. Both reactions are involuntary: the first depends upon a healthy primary center and routes; the second upon a healthy cortical center and routes.
>
> If the patient flinches from the light suddenly thrown on one eye, we know that he sees it, the other eye being closed. If he does not flinch we know that the eye is blind. If the pupil contracts to light, it vouches for the integrity of the reflex mechanism. If the pupil does not contract the reverse may be inferred—viz., that the arc is not intact. If the pupil does not contract to the light, but its fellow iris does, even though it be shaded therefrom (consensual reflex), we know that the afferent tract to the primary optic center is available, but that there is some failure of the third nerve on the same side. We also know that the third nerve on the other side is not affected. If there is no consensual reflex in the other eye, we know that there is something wrong either with the centripetal route of the first eye or the centrifugal tract of the second. If there is no pupillary contraction when we flash the light into both eyes and no closure of the lids, we know that both eyes are blind. Although closing the lids when a strong light is thrown upon the eyes is proof that the light is seen, in hysteria and neurasthenia when this reflex occurs it is possible for the patient to be unconscious that he sees it. The pupillary reflexes may be present in bilateral amaurosis of cortical or subcortical origin and in hysteria; but they are abolished in bilateral amaurosis of peripheral origin.

In the Schmidt-Rimpler test the candidate is instructed to look at his hand while holding it in front of his face. A blind man will look as required, but a malingerer will look in any direction but the right one. This test is not foolproof, however, since a blind man may intentionally look in the wrong direction to avoid arousing suspicion that he can see. A modification of this test is to have the candidate touch the tip of the nose with the finger. These tests should

be tried first with the eyes open and then with one eye or the other covered.

In Smith's modification of the von Weltz test a candle is placed in the subject's line of vision; then it is determined whether the eye converges when a prism of 10 diopters base out is placed before it.

Electroencephalography is now used as a reliable method of distinguishing true and false blindness.[5] If sight is present, the alpha waves are obliterated as soon as the eye is opened.

In the optokinetic nystagmus test (Bach), if the eye is not blind, nystagmic movements will occur when the subject looks at a moving object, such as an automobile, or at striped paper or at some point on a revolving drum.

In Cuignet's visual field test the examiner passes a candle or some other test object across the fields of vision of the two eyes. The dishonest subject denies having vision in the nasal field of the sound eye.

3. Simulated Monocular Amblyopia: Monocular amblyopia is a frequent source of ocular malingering, since persons with slight amblyopia may be guilty of intentional exaggeration. In all cases of suspected monocular amblyopia, faking must be considered and methodically ruled out. It is of the utmost importance to separate the amblyope with corrected vision of 20/40 or better from candidates with more serious amblyopia. The uncorrected vision of the amblyopic eye and the visual acuity of the better eye acting as decisive factors, this differentiation may mean full military service instead of limited duty or limited duty instead of rejection. Table 2 gives the analysis of 44 cases of bona fide monocular amblyopia (1.8 per cent of 2,400 consecutive cases). In 70 per cent there was no squint, and in 30 per cent, monocular esotropia.

Although none of the subjects with esotropia had corrected vision of 20/40, 48 per cent of all the other examinees, mostly those with ametropia, possessed vision which could be corrected to this value. Spherical anisometropia indicates a difference of 3 D. or more in the spheres of the two corrective lenses; cylindric anisometropia, a difference of 3 D. or more in the cylinders, and spherocylindric anisometropia, a combined difference of 3 D. or more in the spheres and cylinders.

The procedure of proving or disproving the existence of monocular amblyopia may be divided into three steps: (1) history taking and routine examination, (2) determination of the presence or absence of prism diplopia and (3) application of the binocular tests for malingering.

5. Lemere, F.: Electroencephalography as a Method of Distinguishing True from False Blindness, J. A. M. A. 118:884 (March 14) 1942.

Step 1: History taking and routine examination: The following questions should be asked: "Did you always have a lazy eye?"; "Were you cross eyed as a child?"; "Did you ever have an operation, an injury or any disease of the eyes?" Examination must include a screen cover test for near and for distant vision, with and without glasses. A number of cases of positive amblyopia (amblyopia ex anopsia and amblyopia due to organic disease) will thus be eliminated. Persons with definite defects are not prone to exaggeration. If there is any doubt, however, the good eye may be occluded, and procedures 2, 3, 4 and 5, as listed under "Simulated Binocular Amblyopia," may be tried. Subjects with alternating squint for both near and distant vision may be treated in the same way. If the candidate reads the 20/20 line at a distance of 11 feet (3.3 meters), his vision is 20/40.

TABLE 2.—*Analysis of Forty-Four Cases of Monocular Amblyopia*

	Corrected Vision		
Monocular Esotropia for	20/40	20/50 to 20/100	20/200 or Less
Near and Distant Vision *	0	7	6
Emmetropia	..	3	..
Cylindric anisometropia	5	2	1
Spherical anisometropia	1	1	1
Spherocylindric anisometropia	3	1	..
Hyperopia	2	3	..
Compound hyperopic astigmatism	2	2	1
Hyperopic astigmatism	2	1	..
Total	15	20	9

* In 5 of these cases there was compound hyperopic astigmatism, and in the others, only slight refractive errors.

Step 2: Prism diplopia: In order to see whether a 10 D. prism placed base up or base down before either eye will elicit artificial vertical diplopia the subject should be instructed to fix on a white pinhead (3 mm. or so in diameter) 33 cm. away. The same test is tried with the subject fixing on a white circle approximately 2 inches (5 cm.) in diameter at a distance of 20 feet. If diplopia is constant and present for both near and distant fixation, the candidate is ready for the binocular tests described under step 3. If the induced diplopia is present only for distant vision, there is probably a squint for near vision, and unless this can be temporarily taken care of by a prism, the binocular tests must be carried out at distances beyond the point of monocular vision. In cases of diplopia for near vision only the reverse holds true.

Inconstance or absence of prism of diplopia calls for the use of a stronger fixation stimulus, such as a muscle light at 20 feet or a flashlight as the near point of fixation. Once diplopia is established by use of a stronger stimulus, the weaker stimuli should again be tried. If diplopia is

established, the candidate goes on to step 3. Often the malingerer will admit diplopia only when the prism is placed over the good eye because he thinks the prism has the power of inducing monocular diplopia.

If the examiner fails to produce any diplopia, malingering (false denial of diplopia) must be ruled out by the following tests:

(1) Von Weltz test. While the subject is reading aloud with both eyes open, a prism of 10 diopters is placed base out before the allegedly amblyopic eye and it is noted whether the eye turns in (antidiplopic movement). This response is compared with that when the prism is placed in front of the better eye.

(2) Duane test. While the subject continues to read, a prism of 4 diopters is placed base up or base down before the alleged poor eye. If the candidate is malingering, he cannot continue without the hesitation created by the vertical diplopia.

(3) Von Graefe test. This test may be used to prove to the candidate that diplopia may be monocular. The subject fixes on a point while the allegedly amaurotic eye is covered. A prism of 10 diopters is then placed before the good eye so that the base bisects the pupil horizontally. As a result, two images are seen, the true one through the uncovered portion of the pupil and the false one through the prism. Slight rotation of the prism will result in motion of one of the images, the other remaining stationary. The other eye is then uncovered, and simultaneously the prism is brought entirely in front of the pupil. If two images can still be seen, binocular diplopia must exist. When considerable anisometropia is present, this test may be made more effective by fogging the sound eye.

These three supplementary tests must be applied to distant, as well as to near, vision, since simultaneous binocular macular perception may be present in one instance and not in the other.

Step 2, then, differentiates the candidates with and those without prism diplopia. The eyesight of the latter is so poor that malingering is not likely. Here, again, if any doubt exists, the good eye may be occluded, and procedures 2, 3 4 and 5 as listed under "Simulated Binocular Amblyopia" may be attempted.

Step 3: Binocular tests: The existence of simultaneous binocular macular perception having been established, the examiner may now attempt to demonstrate the true visual acuity of the allegedly defective eye. The binocular tests are based on the assumption that the subject does not appreciate which of his two eyes is functioning. Consequently, the malingerer can outwit the examiner by closing the eye in question so as to get an idea of what his vision should be if that eye were really defective. He should be cautioned to keep both eyes open, and he must be kept under constant surveillance.

(1) Fogging tests. The good eye may be fogged for near and for distant vision by means of spherical lenses, cylinders, polaroid lenses and colored charts and lenses. The test is always begun with the corrective lenses in the trial frame.

(*a*) Spherical lenses. The good eye is fogged with a + 3.00 D. or a + 4.00 D. sphere, and a balance glass is placed over the bad eye. A 10 diopter prism placed base up or base down over either eye will give vertical diplopia, which will further confuse the malingerer. He is then asked to read down as far as he can, first, on the upper chart and, then, on the lower chart. The "defective eye" is covered, and the degree of reduced vision is checked in the eye that is fogged.

(*b*) Harlan test. A + 6.00 D. sphere is placed before the corrected good eye, so that it is made artificially myopic, with the far point 17 cm. away. The subject is asked to read a Jaeger card at this distance, and then slowly and imperceptibly the card is drawn away. If he continues to read, he is using the "poor eye."

(*c*) Jackson test. A + 4.00 D. sphere is placed before the corrected "bad" eye, and a + 2.00 sphere lens before the corrected good eye. The patient is given a card of small test types to read, and by his reading distance one can tell which eye he is using.

(*d*) Cylindric lens test (Jackson). A + 5.00 D. cylinder and a — 5.00 D. cylinder with the axes vertical are placed before the better eye; as one lens neutralizes the other, there is no change in vision, and the patient satisfies himself that this is so. The necessary corrective lenses are placed before the other eye, and while the subject reads the test types from the larger to the smaller, the examiner interrupts several times ostensibly to adjust the glass before the poor eye, but in reality to change the axis of one of the cylinders in front of the good eye in order to fog it. If the axes are 15 degrees apart, the eye is fogged to a visual acuity of 20/200 or less. If the smaller test types are read with the eye adequately fogged, malingering is proved.

(*e*) Polaroid test (Gradle).[6] Three polaroid disks, 36 mm. in diameter and 2 mm. thick, are placed in a trial frame. One disk is placed before each eye with the polarizing axis horizontal. The patient is asked to read the line of the

6. Gradle, H. S.: Another Test for Malingering, Am. J. Ophth. **20**:300 (March) 1937.

smallest possible letters on the test chart with both eyes open. Immediately the third polaroid disk is rotated so that the polarizing axis becomes vertical for the length of time that it takes to read three or four letters. The rotation of the third disk to the vertical position prevents the passage of any light, so that if the reading of the test chart is continued during this time it is evident that the patient is using the allegedly bad eye.

(*f*) The Project-O-Chart polaroid test.[7] A polaroid disk is placed in the projector and rotated by a handle. The patient wears a pair of spectacles containing polaroid filters, one at axis 90 and the other at axis 180. When the disk is rotated in the projector to axis 90 or axis 180, the letters become invisible to one or the other eye. It has been found that the head must be held motionless, for the slightest movement or tilt to the right or to the left will alter the effect of the polarizing lenses.[8]

(*g*) Fogging by use of colored charts and lenses. This test may be carried out in several ways. In the Snellen glass color chart the letters are alternately red and green. Complementary red and green lenses are placed in the trial frame, and the patient can see the red letters only through the red glass and the green letters only through the green glass. One may modify this scheme by making a test chart for near vision in which a red and a black pencil are used and the colors of the test types are alternated. A red glass placed over the good eye obliterates the red letters, and if any red letters are seen, it is with the "poor eye." In the Delaney chart one letter of each line of the Snellen chart is red. The Wagner chart consists of black and white letters on a pink background. The letters are of such size that the chart is best used at 10 feet (3 meters). A red glass before the good eye will obliterate the white letters. All the letters will be seen if the other eye is normal.

(*h*) The bichrome, or duochrome, test, which is sometimes used in refraction to determine undercorrection or overcorrection, can be utilized by a red glass being placed over the good eye. This will dim out the letters on the green side, so that all the letters read on the green background are seen by the allegedly poor eye. If the subject is color blind, fogging by means of color cannot be done effectively. Vision in the better eye is then checked to determine the extent of the fogging.

(2) Bar test (Javal-Cuignet). A ruler 1¼ inches (3.2 cm.) wide is interposed vertically midway between the two eyes at a distance of 4 to 5 inches (10 or 13 cm.), and the man is directed to read from a printed page with lines at least 4 inches long. If he is able to read the lines, binocular vision exists, and the poor eye cannot be amblyopic.

(3) Harman test. The Harman diaphragm apparatus consists of a rod 18 inches (45.7 cm.) long. At the distal end is a rack to hold the small test type cards, and 4½ inches (11.4 cm.) nearer the eye there is a screen, measuring 3¼ by 2¾ inches (8.3 by 7.9 cm.), which is perforated by a window ⅝ inch (1.6 cm.) square. Beneath is a handle, which is held with both hands; the proximal end of the instrument rests against the upper lip. This apparatus may be modified to fit individual needs. I use a perforated window 1¾ inches (4.5 cm.) wide and 2½ inches (6.35 cm.) high, so that the subject can see all of the different size test types on a 4½ by 5 inch (11.4 by 12.7 cm.) card without further adjustment of the window. One may decenter the window slightly toward the allegedly poor eye. As the patient looks through the opening in the diaphragm, the middle part is seen with both eyes, the right side by the left eye and the left side by the right eye. If the candidate reads across the entire page, he is using both eyes. The fact that the vision is crossed, and not homonomous, will serve to confuse the malingerer, who may choose to read only the print on the side of his good eye. If slight amblyopia is suspected, the good eye may be fogged slightly and the subject asked to read a paragraph of the larger test types. In this instrument there are no eye pieces to hide intentional closure of one eye. Confirmation of binocular sight may be found in the patient's statement that the middle letters or words overlap or are doubled or that individual paragraphs appear on different planes.

(4) Worth amblyoscope test. The tubes are approximated so that the images are crossed. With small test type cards (Gifford)[9] the subject is asked to read from one and then from the other. The malingerer will assume that the images are uncrossed and read the card on the same side as the good eye. If slight amblyopia is suspected, one may fog the good eye slightly and use some of the larger test types. The examiner must make sure the subject does not close one eye and thus discover the ruse of the test.

(5) Measurement of depth perception. Since depth perception is poor in cases of monocular amblyopia, a quantitative test for the acuity of binocular stereopsis, such as that described by

7. The equipment for this test is made by the American Optical Company, New York.

8. Pincus, M. H.: Personal communication to the author.

9. These test type cards may be obtained from the Riggs Optical Company, Chicago.

Dr. Verhoeff,[10] yields valuable information. Few malingerers will suspect that binocular vision is required.

The acuity of binocular stereopsis is reduced by unequal accommodation of 0.5 diopter or more and unequal corrected vision for a line or more of a Snellen chart. Therefore if maximum performance is to be attained, the candidate must wear the proper corrective lenses.

In table 3 the results for 150 subjects are analyzed. The cases on this list were not selected haphazardly, but had to satisfy the following three criteria:

1. Presence of prism vertical diplopia at a distance of 1 meter and less.

2. Vision correctible to 20/20 in at least one eye.

3. Presence of one or more of the following defects:

(*a*) A refractive error in both eyes, such as compound hyperopic astigmatism, hyperopia, compound myopic astigmatism, mixed astigmatism or anisometropia.

(*b*) Muscle imbalance or a history of esotropia in childhood, with or without operation.

(*c*) Defective vision in one eye from organic or other causes, e. g., choroiditis, opacities of the lens and cornea and amblyopia due to anisometropia or monocular ametropia.

TABLE 3.—*Acuity of Binocular Stereopsis in One Hundred and Fifty Consecutive Cases*

Acuity of Binocular Stereopsis	Visual Acuity in the Poorer Eye					
	20/20	20/25	20/30	20/40	20/50 to 20/70	20/100 or Less
20/20 or better * (100 cm.)	21	..	..	..	..	..
20/25 (80 cm.)	18	..	3	2	..	..
20/30 (66 cm.)	8	1	2	8	..	..
20/40 (50 cm.)	12	3	3	8	2	2
20/50 (40 cm.)	2	..	2	3	1	2
20/60 and 20/70 (33-29 cm.)	5	..	2	11	4	..
20/100 (20 cm.)	..	1	2	4	2	6
20/200 or less (10 cm.)	..	..	..	1	1	8
Totals	66	5	14	37	10	18

* This corresponds to a binocular parallactic angle of at least 32 seconds, the interpupillary distance being assumed to be 63 mm.

Conclusions pertinent to the use of this test in the detection of malingering are as follows:

1. An acuity of binocular stereopsis of 20/20 precludes a visual acuity in the second eye of less than 20/20 with corrective lens.

2. An acuity of binocular stereopsis of 20/25, 20/30 or 20/40 usually means that the corrected vision in the second eye is 20/40 or better.

3. An acuity of binocular stereopsis of from 20/50 to 20/70 suggests that the corrected vision in the second eye is between 20/20 and 20/70, but with few exceptions it will be 20/40 or better.

4. Poor acuity of binocular stereopsis does not necessarily mean poor visual acuity in the second eye.

Negative Malingering.—The necessary precautions are the same as those described for negative malingering of uncorrected vision.

III. ORGANIC DISEASE

Positive Malingering.—During World War I hundreds of conscripts of the Russian and Austro-Hungarian empires escaped military service by wrapping their eyes in cloths infected with the secretion of trachomatous patients.[11] Even today, draftees feign chronic conjunctivitis by application of irritating substances. Weekly rechecks by the Army ophthalmologist rapidly discourage a repetition of this form of malingering. The severity of recurrent superficial keratitis is sometimes exaggerated, as both examination and affidavits will testify.

Opacities of the cornea, lens and vitreous, present years after active inflammation has subsided, may disqualify a candidate because of interference with vision. It is often difficult to judge exactly to what extent an opacity in the ocular media reduces vision, and while the obviously honest candidate offers no problem at all, the possible malingerer must be handled in the same way as the man suspected of feigning amblyopia. The same holds true of men with old healed retinitis and chorioretinitis. Although the macula could no longer be identified with the ophthalmoscope, several selectees surprised me by showing corrected visual acuity of 20/25 or 20/30. Others with paracentral chorioretinal scars and intact maculas claimed poor vision, but subsequent tests revealed them all to be malingerers. The test for acuity of binocular stereopsis was especially useful in this group of candidates.

Paralytic squint is rarely feigned and cannot be maintained in all the cardinal directions. An examinee who at first failed to show any extraocular movements except convergence later demonstrated them. While he maintained fixation on a central point, his head was rotated from side to side and up and down by the examiner.

Monocular diplopia is rarely, if ever, simulated. Binocular diplopia is more common, and

10. Dr. Verhoeff[2] has described a simple and accurate device, which can be easily made at home. The degree of stereopsis is measured by the distance at which a depth of 2.5 mm. can be appreciated with standard size test objects. The acuity of stereopsis is expressed in the familiar Snellen fractions. At a distance of 1 meter visual acuity is 100/100, equivalent to 20/20 in Snellen notation, and at a distance of 0.5 meter, 50/100, or 20/40 in Snellen notation. Dr. Verhoeff stated that further standardization is desirable.

11. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1596

is usually easy to detect with the use of a red glass before one eye. The two images can be fused by use of a prism. If the diplopia is real, the subject will admit that the two images have approximated or have fused. The malingerer will persistently claim double vision. Another method of detection is measurement of the degree of stereoscopic vision, which may be found within the range of binocular vision. If the diplopia is present only in one field, the depth perception in that field can be measured.

Ptosis, unilateral or bilateral, is checked by moving the examinee's head down while central fixation is maintained. In another test the thumb is placed firmly on the patient's brow, and he is instructed to look up. In a case of real ptosis the occipitofrontalis muscle will show contraction.

The gravitational test consists in placing the subject in a dental chair and tilting the body and head backward until the ptotic lid drops back by force of gravity. The malingerer, unaware of this ruse, will persist in voluntarily keeping his lid down.

True blepharospasm is temporarily overcome by instillation of an anesthetic, such as 0.5 per cent tetracaine hydrochloride, into the conjunctival sac, whereas simulated blepharospasm persists.

In detection of malingering of changes in the visual fields, different distances and size objects should be employed at one sitting and the tests repeated on several occasions. Inconsistencies are suggestive. Glaucoma, optic nerve atrophy, retinitis pigmentosa, other organic diseases and hysteria must be ruled out.

Negative Malingering.—In the routine examination of selectees and officer candidates the following diseases were discovered, despite the fact that the history was intentionally withheld: chronic simple glaucoma; absolute glaucoma; chronic low grade iridocyclitis; chronic active choroiditis; recurrent uveitis (inactive at the time of examination but recurrent annually for the past four years); retinitis pigmentosa; optic nerve atrophy, due to excessive use of tobacco and inadequate diet; diabetes mellitus and retinal hemorrhages, and, finally, essential hypertension with vascular changes in the retina. Routine ophthalmoscopic examination, particularly of candidates over 30 years of age, with special attention to the caliber and reflexes of the main retinal arterioles and their primary branches, will not infrequently result in discovery of cases of essential hypertension. Although the first blood pressure reading may be within the prescribed limits of normal and the candidate insists that his blood pressure has always been low, several additional readings are indicated. The correlation of ophthalmoscopic observations with several readings of the blood pressure on different days is higher than with the initial reading alone.

IV. DEFECTS IN COLOR VISION

Positive Malingering.—Since color vision is tested only in examination of candidates for commissions, this type of malingering is uncommon. The deuteranope, the protanope and the tritanope, with partial or complete color blindness, make characteristic errors in the pseudoisochromatic tests, and they will read some of the confusion numbers. The use of colored filters, red, green and others, once the examiner has obtained a key by recording their effect on honest normal and color-blind persons, may help in the detection of malingering. The malingerer will rarely make errors in the lantern and Holmgren yarn tests characteristic of the color-blind subject without some revealing blunder. Furthermore, the degrees of subnormal performance in these various color tests will not be consistent. The attitude of the honest examinee toward his perceptual defect and his behavior during the examination are characteristic and cannot be simulated.

Negative Malingering.—Two or more pseudoisochromatic books should be available for presentation. The plates are shown out of their regular order, upside down or only in part, i. e., one letter of a two letter plate. Again, if familiarity with all the plates is suspected, filters may be used once a key has been made. The Holmgren test results in the detection of about 80 per cent of candidates who are incompletely red blind or incompletely green blind to pseudoisochromatic plates and 100 per cent of those who are completely green blind or completely red blind.

However, candidates with complete green blindness or complete red color blindness by studying shades can learn to simulate incomplete red blindness or incomplete green blindness, and therefore the Holmgren test alone is inadequate when malingering is suspected and this differentiation must be made.

A recent report[12] has stressed the value of the William lantern test. If this is not available, the Project-O-Scope test can be used for confirmation. The 1215-2 standard Project-O-Scope slide, which contains a row of four dots —red, yellow, green and blue—is used, and the respective colors can be varied by passing the red and green filters of the selector slide over them.

12. Schwichtenberg, A. H.: Review of Color Vision, with Some Practical Suggestions for Medical Examiners, Arch. Ophth. **27**:887 (May) 1942.

PROLAPSE OF THE UVEA

TREATMENT AND SIGNIFICANCE IN INTERPRETATION OF SYMPATHETIC OPHTHALMIA AND GLAUCOMA

RUDOLF DENIG, M.D.
NEW YORK

I. TREATMENT

In cases of early prolapse of the iris a definite line of procedure has hitherto been followed, namely, careful excision. It will be seen that this rule cannot be strictly adhered to, and must be departed from in certain cases.

In cases of prolapse of longer duration, more than ten days, I suggested, in 1927, that a distinction be made between the noninflammatory and the inflammatory type, the former to be left undisturbed but the latter to be rendered harmless by an iridectomy on both sides. This is the procedure which I have designated as "isolation."

In treatment of prolapse of the ciliary body Coover [1] and Scheffels [2] contributed pioneer service, as indicated by Olah [3] in his article on puncture wounds of the ciliary body. They saved the injured eyeball and achieved smooth recovery by gently freeing the prolapsed ciliary body from its surroundings and excising it—in other words, by employing exactly the same procedure which is now used in cases of early prolapse of the iris.

This, however, does not adequately solve the problem of the procedure with prolapse of the ciliary body. It must be regarded as an error in technic to attempt or to perform excision in all cases, without selection. Clinical experience, the various operations for glaucoma, isolation, iridotorsion and the results in the case of subconjunctival prolapse of the ciliary body due to an incision wound of the sclera, to be described later, indicate, rather, that the procedure in cases of prolapse of the ciliary body and iris must depend, on the one hand, on the nature of the scleral wound and, on the other, on the normal or injured condition of the prolapsed uvea.

Scleral wounds may be classified as cleancut incision wounds, puncture wounds and irregular, lacerated wounds. Prolapses of the uvea may, furthermore, be classified as those in which the tissue is initially uninjured and remains uninjured; those in which the tissue is initially uninjured but subsequently becomes damaged, either by irregular, jagged scleral edges during the course of healing of the wound or later, sometimes after many years, as a result of cicatricial traction or pressure, and, finally, those in which the tissue is initially lacerated.

In this paper are presented a series of possible combinations of scleral wound and prolapsed uvea and consequent variations in procedure, both of which must be considered from the point of view of the possibility that the coincidence of irritation caused by the scleral wound and uveal injury may become the cause of uveitis. The various possible combinations are as follows:

1. Cleancut, incised scleral wound with injured uvea: The irritation proceeding from the scleral wound during the process of cicatrization is sufficient to induce traumatic, nonbacterial, chemotactic uveitis in the injured uvea.

2. Jagged, irregular scleral wound and uninjured uvea: The jagged edges of the scleral wound may cause tears, irritation and inflammation of the uninjured uvea.

3. Jagged, irregular scleral wound and injured uvea: Here both conditions are present from the beginning.

4. Cleancut incision wound involving only the sclera, without injury to the uvea: This combination should not produce inflammatory symptoms. For the iris, this absence of involvement is proved by the result of the incarceration operation for glaucoma, and for the ciliary body, by the following case.

On *June 13, 1936,* I. R., a woman aged *67,* during an operation on the *right* upper eyelid, believing that the procedure was *finished,* suddenly *jerked* her head forward, in an effort to get up from the operating table. Immediate examination of the eye showed that the Graefe knife, with which the pedicle of the tumor had simultaneously been cut, must have *slipped* through the lid and upward beneath the conjunctiva, cutting the sclera about 3 mm. from the corneal margin, between *10:30* and 1 o'clock. I saw the lips of the scleral wound suddenly open and the uninjured ciliary body prolapsing. The amount of the prolapsed tissue increased visibly until it attained the size of a pea. Beneath the stretched conjunctiva it resembled, except for its dark discoloration, a subconjunctival luxation of the lens.

1. Coover, A.: Ophth. Rec. **12:**179, 1903.
2. Scheffels, A.: Klin. Monatsbl. f. Augenh. **45:**396, 1907.
3. Olah, E.: Klin. Monatsbl. f. Augenh. **100:**905, 1938.

This case was a model example of incarceration, with smooth edges of the scleral wound and an intact uvea, a combination which, according to the foregoing classification, is to be regarded as harmless, and not requiring excision of the prolapsed tissue. The subsequent course in this case confirmed such a belief, for at no time did the slightest sign of irritation appear, either after the injury or during the subsequent years of observation, nor did the patient ever complain of any sensation of pressure or pain. As always, so at the last examination, on May 23, 1943, vision, accommodation, pupillary reaction and tension were normal. The incipient senile cataract, which was present even before the injury, had made almost no progress. The pupil was round and had the same diameter, 2 mm., as that in the left eye. There was, however, a slight protrusion of the senile, thin upper lid corresponding to the seat of prolapse, especially when the patient looked downward. The prolapsed tissue rested on the sclera, with no irritation whatever.

Subconjunctival incised wounds of the sclera without injury to the ciliary body are extremely rare, whereas nonsubconjunctival wounds are not. In cases of the former one refrains from any intervention, whereas in cases of the nonsubconjunctival wound the procedure will depend on whether the wound is fresh, i. e., of not more than twenty-four hours' duration and, further, on whether the pupil is deformed. If the wound is fresh, a plastic operation on the conjunctiva will suffice to cover the prolapsed portion. If the wound is more than twenty-four hours old, immediate excision is indicated, as it is in cases of fresh wounds that the pupil is deformed. Deformation of the pupil occurs when the injury is located near the limbus.

If in a case of an incised wound the ciliary body is injured, excision must be done immediately and an attempt made to include the corresponding segment of the iris if possible.

The advantage of a conservative procedure in cases of incised wounds of the ciliary body is obvious, as, in order to free the prolapsed tissue, it is necessary to insert the spatula to a depth of 2 mm. between the sclera and the vitreous. In view of the precarious position of the vitreous and lens and the poor visibility of an operative field lying, so to speak, in a dark chamber, in contradistinction to the easily accessible and clearly visible anterior chamber, this procedure is not without danger, quite aside from the fact that some vitreous is usually lost.

In cases of puncture wounds immediate excision is indicated. In such cases the wound is frequently irregular in shape. When the puncture wound is small, it is not easy to get hold of the incarcerated ciliary body. Olah reported a case in which, owing to the extreme narrowness of the puncture canal, he found it difficult to free the ciliary body with a conical probe and then to draw it far enough forward to obtain a good hold. In his case he was able to extract and cut off the corresponding segment of the iris with the ciliary body.

Such efforts must be limited, however, when there seems to be danger of crushing or lacerating the incarcerated uveal tissue with consequent irritation and uveitis. As a warning, the following case of sympathetic ophthalmia following trephination is presented.

A. U., aged 18, whom I saw on June 23, 1933, had glaucoma in the left eye, which had developed after a blunt injury. Trephination yielded only transitory reduction in tension. A few days after operation the *tension began to increase again, as the iris had become* incarcerated. On the tenth day the surgeon who had performed the operation reopened the wound to remove the obstruction, with only partial success. Subsequently sympathetic ophthalmia developed, which in spite of all efforts led to bilateral blindness.

Also, in operations for advancement of extraocular muscles danger of sympathetic ophthalmia may develop if the needle is inserted so deep that uveal tissue is caught in the loop of thread, with resultant laceration, which may lead to iridocyclitis and shrinking of the eyeball. I previously described such a case.[4] With my method of anchoring the suture in the anterior chamber in cases of high myopia with thin sclerotic coats, and also in cases of high degrees of strabismus, such danger is eliminated, as the needle introduced into the anterior chamber remains constantly under the watchful eye of the surgeon. That the thread will lie in immediate proximity to the iris is of no significance, as it is removed in five or six days.

Prognosis is least favorable in cases of lacerated wounds because the uveal tissue is caught in the pockets of the wound and is difficult to remove. Incomplete removal will yield, if any, only a transitory, deceptive respite from symptoms. As soon as regrowth of uveal tissue from the trunk restores the connection with the prolapsed portion, irritation and uveitis will recur, with danger of sympathetic ophthalmia. In cases of subconjunctival rupture of the eyeball, in which the ciliary body as a rule is intact, immediate excision should be attempted. If this is only partially accomplished, however, it must be followed at once by enucleation.

The same procedure is recommended in cases of prolapse associated with injury of the lens and, finally, also in cases of older prolapse of the ciliary body, of more than fourteen days' duration.

With regard to sympathetic ophthalmia, it is the duty of the surgeon to proceed cautiously rather than to risk bilateral blindness, which

4. Denig, R.: Klin. Monatsbl. f. Augenh. **96**:177, 1936.

could be prevented by prompt enucleation. To attempt excision of a prolapsed portion of the ciliary body in all cases involves risk. At least, it will not do to assume that should sympathetic ophthalmia develop, there will be ample time to combat it or, at worst, to perform an enucleation.

Under no circumstances must consideration of the disadvantages of wearing an artificial eye be the determining factor in the decision as to whether one should attempt to save the endangered eye. An attempt at excision appears justified only when the uninjured eye is amblyopic. Even if all goes well for a number of years after such an operation, the end result is far from certain. Coover's patient, for instance, responded favorably at first. Half-vision was preserved, but "after a period of years, recurrent vitreous opacities developed, with slight increase of tension and cataract formation." It is to be assumed that the eye had finally to be enucleated. Unfortunately, in the majority of cases one remains ignorant of the final result.

All this shows the great significance in the development of uveitis of injury of the uvea in connection with the irritation emanating from the seat of its incarceration. In the case previously described, that of subconjunctival prolapse of the ciliary body, the two conditions of integrity of the uveal tissue and smooth edges of the wound were fulfilled, and for this reason the incarceration produced no irritation or inflammation. This is true, likewise, in cases of iridotorsion, except that here the conditions are more favorable because the iris is embedded in a canal. In the incarceration operation of Holth and its modifications the danger of sympathetic ophthalmia is present because the artificially produced prolapse of the iris still further constricts the angle of the anterior chamber, already constricted and shallow as a result of glaucoma. The obstruction of the angle may lead to tears in the originally intact iris, and eventually to sympathetic ophthalmia. Thus cyclodialysis in an aphakic eye, owing to the deeper angle of the anterior chamber, is more reliable. Iridotorsion with the requirement that the base of the scleral wound be 1 mm. in width circumvents all this danger.

In operations for cataract iris tissue incarcerated in an irregular incision may cause irritation and injury of the uveal tissue. In addition, with extracapsular extraction one has to deal with the dangerous irritation due to residual fragments of the lens and capsule, the absence of which with incarcerations following intracapsular extraction explains their relatively harmless character.

In cases of prolapse of the iris the greatest caution must be observed during excision, or here too the uveal tissue will reform from the trunk and grow toward the remnants of the prolapsed portion. This is especially true of prolapse of the iris with irregular, jagged edges of the wound. Such wounds constitute the deviation from the rule previously stated. It is particularly with wounds of this type that one not infrequently hears of the development of sympathetic ophthalmia in spite of accomplished excision. The safest method in such cases, provided the prolapse is not too extensive, is to leave it completely at rest, but to perform a broad iridectomy on both sides, i. e., to carry out the isolation procedure. If, however, one is forced to choose excision in a case of extensive prolapse, subsequent isolation of the site of excision should be effected as soon as possible.

Isolation of a prolapsed portion of the iris consists, accordingly, in complete interruption of its connection with the trunk and its exclusion from the irritation emanating from the seat of incarceration. A bilateral cyclectomy would prove to have the same effect for an old inflammatory prolapse of the ciliary body.

After extracapsular extraction, even in the absence of inflammatory symptoms, when the time for excision has passed, isolation should, in principle, be attempted. Thus, recently I isolated an incarcerated iris pillar after extracapsular extraction in a case in which, after the process had remained quiet for nearly a year, a dangerous inflammatory condition had suddenly developed. Years ago I lost the second eye in 2 cases of incarceration following operation for cataract as a result of sympathetic ophthalmia.

II. ANIMAL EXPERIMENTATION

For these investigations, certain aspects of the ciliary nerves and the sympathetic vascular innervation require particular attention.

Scheffels[5] made the following observations after resection of the ciliary nerves, or neurectomy, in 4 cases of purulent choroiditis following penetrating injury:

> A peculiar antiphlogistic effect of the resection was noted in the presence of suppurative choroiditis. Processes of a most stormy course took on subsequent to resection a chronic, torpid character. The impression was gained that, aside from the absence of subjective symptoms, the acuteness of the inflammatory process itself was considerably changed; . . . the picture suddenly became different.

In this connection, Dreyer and Jansen observed that erythema of the ear of the rabbit produced by light radiation healed more quickly when the sympathetic nerve supply had been partially cut;

5. Scheffels, O.: Klin. Monatsbl. f. Augenh. 28: 197, 1890.

likewise, the observation of Spies and the experiments of Bruce, Hardy and others indicated that limitation of the vascular reaction by anesthesia exerts a favorable effect on the course of experimental inflammation.

Spies,[6] on the basis of clinical observations, stated:

> . . . Inflammation will not become manifest if the reflexes passing from the focus of inflammation to the centripetal sensory nerves can be excluded. . . . An already existing inflammatory lesion will heal rapidly after anesthetization of the focus of inflammation. . . . The anesthetization must involve only the sensory nerves and must not disturb the normal function of the sympathetic (vasomotor) nerves.

ANIMAL EXPERIMENTS OF BRUCE

Bruce,[7] following Spies's line of thought, made the following experiments at the Pharmacologic Institute of the University of Vienna.

1. *Effect on the Inflammatory Process of Transverse Section of the Spinal Cord.*—In order to ascertain whether the inflammatory process takes place within or outside of the anesthetic zone, Bruce treated with mustard oil, croton oil or boiling water a shaved area of the skin in animals rendered partially anesthetic by transverse section of the cord at the level of the tenth thoracic segment. The inflammatory process was not prevented or influenced and was not therefore of cerebral origin.

2. *Effect of Division of the Posterior Roots on the Inflammatory Process.*—This section, too, failed to prevent or modify the usual course of inflammation. The inflammatory process was therefore independent of the integrity of the central and spinal paths.

3. *Experiments on Nerve Endings.*—(*a*) Under the influence of a local anesthetic, of a type affecting only the sensory nerve ends, such as amydricaine, inflammation failed to develop for the duration of exclusion of the sensory nerve ends when mustard oil was instilled into the conjunctival sac. (*b*) The same result followed division or resection of the first branch of the trigeminal nerve from its root ganglion if sufficient time for degeneration was permitted to elapse before instillation.

The experiments of Bruce constitute a confirmation of Spies's theory.

Scheffels[5] was able, furthermore, to demonstrate a peculiar retrogression of a staphylomatous protrusion of the cornea following neurectomy in 2, but not in all, of his cases. The staphyloma, which up to the time of operation had grown progressively, without interruption, subsequently diminished to a degree noticed even by the patient. "The previously greatly increased tension then fell to normal." (Compare this effect with that of retrobulbar injection of cocaine!)

Experiments were conducted by Thiel[8] on reflex variations of intraocular tension in normal and in glaucomatous eyes following stimulation of the sympathetic fibers by way of the ganglion cervicale supremum, the ganglion sphenopalatinum and the tympanic membrane. He observed that unilateral stimulation produced a vasomotor reaction in both eyes and bilateral variations in tension by propagation of the stimulus to the vessels of the choroid.

At the Thirteenth International Ophthalmologic Congress, in Amsterdam, Netherlands, in 1929, in the discussion on transmission of irritation from one eye to the other via the vasomotor reflex, it was demonstrated that there exists a series of vasomotor reflex processes in other paired organs—for instance, heating of one arm leads to simultaneous dilation of the vessels in the other arm (Leriche and Fontaine), and removal of one kidney is followed by reflex anuria in the remaining kidney.

"Direct" and "indirect" vasomotor reactions consist in dilation of the vessels with increased permeability of the walls and slowing of the blood stream. According to Krogh,[9] the direct reaction occurs within the irritated area and the indirect reaction outside this area after a certain period of latency. The latter is due to propagation of the stimulus via the nerve fibers of the capillaries. The reaction is a genuine reflex and may involve a much larger area than the direct reaction—in fact, areas quite distant from those involved in the direct reaction, in this case, the second of the paired visual organs.

In cases of prolapse of the uvea, therefore, the ciliary nerves receive the mechanical stimulus from the seat of incarceration. They transmit it as a "sensory vasomotor reflex" to the sympathetic innervation (vasodilator fibers) of the capillaries, the latter responding with a direct reaction in the first eye and with an indirect reaction in the second eye. The ciliary nerves are therefore the receptors of the stimulus. The sensory reflex is the so-called short axon reflex. The degree of the reaction depends on the strength of the sensory reflex, and this, in turn, on the duration of the irritation, with its possibility of

6. Spies, A.: München. med. Wchnschr. 8:345, 1906.

7. Bruce, A.: Arch. f. exper. Path. u. Pharmakol. 63:424, 1910.

8. Thiel, R.: Klin. Monatsbl. f. Augenh. **82**:109, 1929.

9. Krogh, A.: The Anatomy and Physiology of the Capillaries, New Haven, Conn., Yale University Press, 1922.

summation (Ebbeke), and on its nature and consistency. The most important strengthening of the reactions is attributable, however, to the vasomotor psychoreflex, which functions in the area of the paired trigeminosympathetic ocular plexus in the region of the direct and indirect reactions, to which I shall refer later.

Local irritation has often been suggested as the cause of sympathetic ophthalmia; I shall mention only a few instances. Bach, in 1896, inflicted wounds in the ciliary region in rabbits, which either healed promptly or went on to suppuration, after which the eye rapidly recovered. Moll, in 1898, inserted a sliver of copper into the iris. The ciliary body has, likewise, been spiked with needles and eroded with caustics.

PRESENT ANIMAL EXPERIMENTS

1. *Scarifications of a Unilateral Lacerated Subconjunctival Prolapse of the Uvea.*—These scarifications were made with a discission knife for the purpose of producing recurrent irritation of the uvea. Within two months I made 19 and 20 scarifications respectively, 1 every third day, on 2 brown rabbits—or 39 scarifications in all. The prolapse was produced subconjunctivally with a Graefe knife, in order to avoid danger of infection of the wound—in 1 rabbit a prolapse of the ciliary body of 6 mm., with considerable loss of vitreous, and in the second rabbit, prolapse of the iris of 4 mm. In the first rabbit, i. e., the animal with the loss of vitreous, shrinkage of the eyeball set in after twelve days, without any notable inflammatory symptoms. In the animal with the prolapse of the iris there developed mild iritis, which showed a decided tendency to heal and was associated with a few posterior synechiae. Finally this eye also atrophied. Every scarification—performed without use of an anesthetic—caused severe pain, but shortly afterward the eye was again kept open and was only slightly reddened, without much inflammation. There was no lacrimation. On the day following the scarification only slight crusting of the lids was evident. No sympathetic irritation of the second eye was observed with any of these 39 scarifications.

2. *Scarification of a Bilateral Lacerated Subconjunctival Prolapse of the Uvea.*—(*a*) By the same method as that employed in the scarifications described in the preceding section, the prolapsed portions of the iris and ciliary body of both eyes were scarified in 1 albino rabbit and in 1 brown rabbit. After the injection of the eye had subsided, an attempt was made to bring about irritation of the prolapsed portion in the first eye by scarifying the prolapsed tissue in the second eye. Five such scarifications were made in each rabbit within two and one-half weeks, but they had not the slightest effect on the first eye.

(*b*) When the first eyes of the same rabbits had cleared up, they were scarified seven times within three and one-half weeks in order to ascertain whether the still slightly injected second eyes would respond with intensified injection. But the scarification had no effect, and the rapidly progressing clearing-up process was not delayed.

Of the 4 eyes in experiments *a* and *b*, mild, rapidly subsiding iritis developed in 3 and atrophy without much inflammation in the fourth. There was no evidence that genuine sympathetic irritation resulted from the 24 scarifications in these experiments. To be sure, immediately after the operation transitory hyperemia, lasting five to ten minutes, appeared in the second eye, a reaction which might suggest sympathetic irritation. This was due, however, to the fact that the struggling animal was held and its head pressed on the table during the operation. Mere pressure of a board on the second eye produced the same symptoms, and when scarification was done with the rabbit in the sitting position, no hyperemia developed. Furthermore, it was repeatedly observed that in their cage the rabbits not infrequently bumped against each other, bumped their heads against the wall or rubbed their eyes with their paws, so that occasionally the conjunctiva was superficially injected. The mild closure of the palpebral aperture of the second eye was attributable to natural coordinate orbicular function, and not to photophobia in the sense of sympathetic irritation.

According to the generally accepted assumption, sympathetic irritation and sympathetic ophthalmia have, with respect to their nature and cause, been regarded as two completely different processes, to be sharply differentiated. Schleich,[10] stated: "Whereas sympathetic irritation occurs in animals under the same conditions and with the same symptoms as in man, sympathetic ophthalmia never occurs in animals."

As the most important result of these experiments must be emphasized the rapid subsidence of the sensory vasomotor reflex as compared with that in man and, contrary to Schleich's statement, the absence of sympathetic irritation. Both phenomena are attributable, as will be seen in the "Summary," to the weakness of the congenital vasomotor psychoreflex, which is only rudimentally developed in animals.

10. Schleich, G.: Tieraugenheilkunde, Berlin, Julius Springer, 1922, p. 165.

In experiments 1 and 2, unilateral and then bilateral stimulation of the sympathetic ganglions could be combined, as was done unilaterally by Thiel in both normal subjects and patients with glaucoma. Such stimulation of the ganglions, however, would be of help in the present investigation only if it were possible to keep up prolonged, continuous irritation, lasting not for a short time and subsiding rapidly, but persisting for weeks.

3. *Unilateral Lacerated Subconjunctival Prolapse of the Uvea; Strengthening of the Sensory Vasomotor Reflex by Psychic Influence*:—A year old, extremely nervous, dog, of mixed breed (cocker spaniel and Spitz) was confronted by a cat twenty-three hours after operation on the left eye, which was combined with incision of the capsule of the lens. The cat was held by an assistant, Mr. S. Seach, and the dog was held by Miss Daisy Mapes, while I held the dog's head. The cat and the dog were brought near each other and then withdrawn in rapid succession, the assistant striking the left side of the dog's jaw with the cat's right paw, an act which caused the dog to snap with fury. The experiment was repeated with other cats, and each time an examination, made immediately, showed pronounced reddening of the intact eye, which subsided after the fight was interrupted. The hyperemia thus induced was not distributed equally over the eyeball, but was sometimes more pronounced in the upper, and sometimes in the lower or the lateral, region. It could not have been induced mechanically by barking, for the dog did not bark; he was too busy snapping. Also, I was careful to keep my hand holding the head far from the ocular region, so that any pressure on the eyeball could be excluded. None of the cats showed any injection of the eyes.

I therefore feel justified in claiming that the injection appearing in the dog's intact eye was produced by psychic influence, causing a visible indirect reaction in the nature of a genuine mild sympathetic irritation (see "Summary," sections 7 and 8).

This experiment was made in the department of surgery and surgical pathology, Columbia University College of Physicians and Surgeons, on Oct. 25 and 26, 1943.

INTERPRETATION

From the preceding sections of this paper the following conclusions may be drawn: *In cases* of prolapse with intact uvea, the sensory vasomotor reflex released by the mechanical irritation is capable, at most, of producing increased tension in predisposed eyes. Inversely, in the presence of glaucoma, operative prolapse, with a loose conjunctival flap, may, by intraocular tension, favor the formation of extremely fine fissures and canaliculi, so that tension is decreased (Denig [11]). Occasionally sympathetic irritation of the second eye may be seen. This may persist without danger of sympathetic ophthalmia so long as no injury to the uvea of the first eye (tears) develops.

In cases of prolapse with injured uvea, there occur chemotactic irritation and inflammation of the injured site as a result of the direct reaction, the decomposition products of which may be carried by the blood stream to distant parts of the uvea, with resulting uveitis. The dilation of the vessels, likewise occurring with the indirect reaction, with the slowing of the blood stream, affords opportunity for lodgment of a metastatic focus of chemical decomposition products from the area of uveitis in the first eye to the capillary network of the second eye. These products, on reaching the second eye, release a direct reaction via the sensory vasomotor reflex, with resultant sympathetic ophthalmia.

In cases of jagged scleral wounds, even without incarceration of the uvea, uveitis may develop after an interval of years, in which case one must assume subsequent injury from tears due to cicatricial traction or pressure.

Also, in cases of sympathetic ophthalmia following subconjunctival rupture of the eyeball, the jagged edges of the scleral wound may cause irritation and inflammation in the presence of simultaneous tears of the uvea or, if such tears are produced subsequently, in the course of cicatrization. In the great majority of cases the irritative process is located between the edges of the wound and their immediate vicinity, or more distantly if the injury of the uvea is deeper. Under the latter condition a picture may develop described by Redslob as the "primary lesion" of an infection which he assumed to be ectogenous. The objections to Redslob's theory of a primary lesion are known (Fliri [12]), and only too well justified, and will not serve to account for sympathetic ophthalmia as a bacterial infection. My interpretation of uveitis of the first eye as a chemotactic inflammatory process explains the presence of small foci of infiltration scattered irregularly over the uvea. Whereas the chemotactic inflammatory process is associated with the surfaces of the wound of the injured uvea by its very nature, and therefore remains purely local, its chemical decomposition products may be scattered irregularly through the uvea by the capillaries. This spread will of course depend entirely on whether the capillaries in question

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11. Denig, R.: Arch. f. Ophth. **125**:156, 1930.
12. Fliri, A.: Ztschr. f. Augenh. **55**:27, 1925.

have in the meantime become degenerated by rapidly developing cicatrization and obliteration or have been cut off from the capillary system altogether. If this has occurred, as is usually the case, such an eye may, notwithstanding, be greatly irritated by cicatricial traction. Reis [13] drew attention to the fact, as did Gilbert,[14] that anatomic studies of severely injured eyeballs with extensive incarceration of the iris, which had finally to be enucleated because of violent, uncontrollable inflammation, surprisingly often showed no intraocular process corresponding in degree to the violent external inflammatory condition, the intraocular tissues appearing to be wholly free from such changes. I can only confirm the observations of Reis and Gilbert. Such eyes remain always dangerous, however, because of the possibility of subsequent tears of the uvea due to cicatricial traction.

In all cases the intrinsic defensive forces of the eye make an effort to effect healing. They are nearly always successful, so that the danger of sympathetic ophthalmia is decreased. This pertains to panophthalmia and to perforated corneal ulcer as well. That these conditions only rarely lead to sympathetic ophthalmia is due not only to the absence of jagged edges of the perforation into which the iris prolapses but to the barrier offered by these defense forces of the eye by a wall of leukocytes and indurations. In their effect these processes resemble my isolation procedure. I refer to the beautiful specimen presented by my teacher von Michel.[15] In a similar manner, I was able to demonstrate with reference to the behavior of foreign bodies in the anterior chamber of the rabbit [16] that small brass slivers surrounded by a covering of leukocytes were well tolerated, without signs of irritation of the iris during their migration. Here, one should also mention the so-called ossification of the choroid, which is due to formation of bone in the indurations, and is therefore harmless. However, the defense mechanism may fail, especially when the vasomotor psychoreflexes are strongly developed. For this reason, it is wise to render prolapse of the uvea harmless by operation as soon as possible. Thus, in cases of early prolapse, of twelve days' duration at most, one should consider excision or isolation or a combination of the two procedures, and in cases of older prolapse, isolation.[17] With these two operations it is possible either to remove the irritation caused by incarceration, with its source, or, what brings the same results, to isolate the focus. Thus the sensory vasomotor reflex is abolished, and the uveitis will heal almost instantly, provided ocular degeneration is not too far advanced.

With regard to neurectomy, it has been demonstrated that even when the nerve endings do not come into direct contact, numerous nerve fibrillae may grow from the nerve stumps into the eyeball and thus restore sensibility.

Excision of the prolapsed tissue, isolation, neurotomy or neurectomy, although discarded because of unreliability, fulfil Spies's [6] requirements:

1. An inflammatory process will not become manifest if it is possible to exclude by anesthetization the reflexes passing from the focus of inflammation to the centripetal sensory nerves. 2. An already existing inflammatory focus heals rapidly after its anesthetization.

One needs only supply for the word "anesthetization" the three operative terms mentioned.

The possibility that one may surgically exclude the irritative focus of the sensory vasomotor reflex, and thus at will check the direct reaction and the uveitis in the affected eye, as well as the indirect reaction, refutes the assumption of a bacterial cause of the inflammation. Unquestionably, it is not a matter of a bacterial or virus origin, but only of chemical decomposition products in the production of traumatic, nonbacterial uveitis, which, in turn, may lead to metastasis to the second eye.

That which excision, isolation and neurectomy do for both eyes, enucleation does for the second, or unaffected, eye. It excludes with the irritative focus the indirect reaction, as well as the focus of metastasis, and thus nearly always prevents sympathetic ophthalmia. If the latter is already present, the operation usually has a favorable effect on its course. In some instances, just as with the isolation procedure in the case of the first eye, enucleation may be too late if the inflammatory process has been present too long and metastasis has already taken place.

In cases in which sympathetic ophthalmia develops in spite of preventive enucleation, the metastasis to the second eye may have taken place before enucleation, and in cases of late inflammation, with the time limit of seven to

13. Reis, cited by Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931, vol. 4, p. 603.

14. Gilbert, cited by Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931, vol. 4.

15. von Michel, cited by Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931, vol. 4, p. 226.

16. Denig, R.: Sitzungsb. d. phys.-med. Gesellsch. zu Würzburg, 1896, p. 75; Ber. ü. d. Versamml. d. ophth. Gesellsch. (1896) **25**:305, 1897.

17. Denig, R.: Klin. Monatsbl. f. Augenh. **79**:599, 1927; **87**:845, 1931; **94**:450, 1935; footnote 4; Isolation for Iris Prolapse, Arch. Ophth. **8**:477 (Sept.) 1932; Iridotorsion: Confirmation of Its Anatomic Basis by Fortin's Investigations on Glaucoma, ibid. **24**:482 (Sept.) 1940.

eight weeks (Schieck[18]) before its appearance, it may be assumed, in accordance with sections 7, 8 and 9 of the "Summary," that with vasomotor psychoreflexes of congenitally poor development, smoldering uveitis may be present for a long time before becoming externally manifest. In exceptional cases the sympathetic process may extend along the emissary or ciliary vessels and nerves through the sclera (Fuchs), so that after enucleation a sympathetic focus of inflammation remains outside the eyeball.

In a small number of cases of sympathetic ophthalmia reported in the literature enucleation was done either immediately or shortly after the injury. These cases cannot be included in my interpretation of sympathetic ophthalmia because in such instances the inflammatory changes in the injured eye could be only in the first stages of development. For this reason, I regard the condition in such cases not as sympathetic ophthalmia but as incidental iridocyclitis. On the other hand, cases of sympathetic ophthalmia associated with necrotic sarcoma of the choroid, zoster necrosis of the iris and jagged intraocular foreign bodies with laceration of the uvea, as well as cases formerly studied after reclination of the lens, may all well be included, because they fulfil the requirements of injury of the uvea and continuous irritation of the uvea.

SUMMARY AND CONCLUSIONS

1. A fresh prolapsed portion of the iris should be excised if the edges of the wound are smooth. If, however, the edges are jagged and irregular and the prolapse is not too extensive, excision is contraindicated, and a broad iridectomy should be undertaken on both sides of the prolapse, i. e., isolation of the prolapsed tissue.

2. If the prolapsed portion has lacerated edges and is too extensive, it should be excised, and the site of excision itself should be isolated subsequently.

3. In the presence of an older inflammatory prolapse of the iris isolation is indicated.

4. A fresh prolapsed portion of the ciliary body with cleancut edges of the wound and intact uvea does not require excision, but calls only for a conjunctival covering. When the uvea is injured excision is required.

5. In exceptional cases of irregular, lacerated edges of the wound with injury of the ciliary body excision may be attempted, but enucleation is the safest procedure in such cases.

6. In cases of sympathetic ophthalmia due to prolapse of the uvea the manner of development of uveitis is the same in the two cases, i. e., lesion of the uvea and continuous irritation. In the first eye the lesion is caused by trauma, and in the second eye, by metastasis of chemical decomposition products from the uveitis in the first eye. In the first eye a continuous mechanical irritation, with a superimposed, stronger chemical irritant, releases a sensory vasomotor reflex via the ciliary nerves. The direct sympathetic reaction thus released by this reflex leads to chemotactic irritation and inflammation of the involved damaged portion of the uvea. The appearance of hypersensitiveness to uveal pigment indicates merely a phase of sympathetic ophthalmia, not its cause. Products of chemical decomposition gain access with lymphocytic infiltrates to the blood stream and are then scattered through the rest of the uvea. In the second eye it is likewise the metastasis which causes not only the lesion but the chemical irritation, releasing in its turn a sensory vasomotor reflex, with a direct reaction.

The indirect reaction, with the associated dilation of the vessels and slowing of the blood stream, clears the way for metastases to the capillary system of the second eye, unless the capillaries have become obstructed by the defense reaction of the first eye. In the uvea of the second eye there is, so to speak, the native soil for development of an inflammatory process exactly like the uveitis of the first eye. If the sympathetic ophthalmia begins as papillitis, one may suspect metastasis in the capillary system of the optic nerve; such a metastatic lesion runs a mild course, because it is in foreign, not in its own uveal, soil.

7. The almost immediate subsidence of iridocyclitis in animal experiments is not attributable to any congenital lesser sensibility to stimuli on the part of the sensory fibers of the first branch of the trigeminal nerve. The strong expressions of pain by the animal during experiments performed without local anesthesia refute this assumption. Rather, as demonstrated in my experiments, the rapid subsidence of the sympathetic reaction, i. e., of the sensory vasomotor reflex, as compared with the duration of the reaction in human subjects, is to be attributed merely to congenital weakness of the primitive vasomotor psychoreflex in animals. The latter is the determining factor in the maintenance and increase of the sensory vasomotor reflex. The lower development of the reflex in animals explains the rapid subsidence of the sympathetic reaction and the consequent freedom from sympathetic ophthalmia and sympathetic irritation.

8. The vascular injection, sensitivity and photophobia, known as sympathetic irritation of the

18. Schieck, F.: Arch. f. Ophth. 95:322, 1918.

second eye, which occur now and again and are noticed by the patient and his friends, have been attributed by Peters[19] to a preexisting exaggerated, purely local, sensibility in the trigeminal area and to a certain nervous disposition, a neuropathic constitution (Römer's traumatic hysteria). Reis expressed the opinion that psychogenic processes are principally involved.

According to my investigations, sympathetic irritation must be interpreted as a manifestation of a congenitally exaggerated psychic sensitiveness by the aid of vasomotor psychoreflexes in the paired areas of the trigeminosympathetic ocular plexus in the region of direct and indirect reactions. The vasomotor reflexes are the instrument of the sensitiveness, and likewise a gage of its degree. The degree of sympathetic irritation is determined by the degree of psychic sensitiveness, which is more pronounced in young persons; its importance depends on the injured or noninjured condition of the uvea. In the presence of a weak psychoreflex, sympathetic irritation may fail to develop, as is frequently observed at the onset of sympathetic ophthalmia. This indicates, however, that even under such circumstances the psychoreflex must be present in sufficient strength to keep the sympathetic reactions functioning, and thus permit development of sympathetic ophthalmia.

At this point, attention is drawn to the psychoreflex of blushing, frequently noticed even by the layman, and to psychic crying, the latter being peculiar to man. Psychic weeping does not occur in the first months of a child's life but appears as the psyche develops, whereas in the highest order of apes, that nearest man, only a whimper can be induced. The reader is further reminded of the range of psychogenic possibilities in the hypnosis experiment by which it is possible in predisposed subjects to produce such a violent exaggeration of the vasomotor reflexes that application of a cold spoon will produce a blister.

9. Next to uveal injury and continuous uveal irritation, the vasomotor psychoreflex constitutes one of the three fundamental factors in sympathetic ophthalmia, in that it prevents rapid extinction of the sympathetic reactions. It also renders comprehensible the variability in the degree of the sensory vasomotor reflex from one man to another and from man to animal, as well as the more frequent incidence and the more serious course of sympathetic ophthalmia in young subjects, a fact which cannot be wholly explained by greater exposure to injuries at this age.

10. This new interpretation of sympathetic ophthalmia was suggested to me by the isolation operation, undertaken at first in a case of secondary glaucoma due to incarceration of the iris following extraction of cataract by the combined method. In this case, only complete isolation of the irritative focus by a second iridectomy on the other side of the incarcerated pillar produced complete paralysis of the sympathetic reaction, i. e., the sensory vasomotor reflex, with resulting normal tension. This case illustrates the great importance of the procedure. This observation encouraged me to extend the isolation operation, in contradiction to the ophthalmologic A B C of nonintervention in the presence of uveitis, to cases of iridocyclitic irritation and inflammation, with the same good results. This experience confirmed Spies's observations and the experimental results of Bruce and explained the effect of neurectomy, excision of prolapsed uveal tissue and enucleation of the affected eye. In each case it yielded with the certainty of an animal experiment the same surgical confirmation of the accuracy of the fundamental theory. Subsequently, a distinction between uveal prolapse with tissue injury and one without, as well as further animal experiments, yielded more information indicating the association of the three aforementioned factors in the development of sympathetic ophthalmia.

11. In primary glaucoma, also, the vasomotor psychoreflex constitutes one of the three etiologic factors. In the early stage of glaucoma a stimulus, caused not infrequently by vascular changes, induces a sympathetic reaction. Only after superimposition of the vasomotor psychoreflex on the vasomotor sensory reflex is the intraocular secretion of fluid increased to such a degree that, on the assumption of an already existing or developing obstruction of the outlets of the eye, the mechanism for increased intraocular pressure is started. The degree, nature and course of the hypertension will depend principally on the congenital degree of strength or weakness of the psychoreflex, the age of the patient, his general condition and the state of his eye in particular.

In acute glaucoma hypersecretion in itself may induce an attack, owing to too rapid propulsion of the iris-lens diaphragm, with its resulting compression of the angle of the anterior chamber (see page 234 for the effect of cyclodialysis on the aphakic eye).

In juvenile glaucoma, appearing in the first or second decade, congenital hypersecretion is involved. This is in line with the not infrequent

19. Peters, A., in Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, ed. 3, Leipzig, Wilhelm Engelmann, 1919.

coincidence of other congenital anomalies (Löhlein[20]). Also, the prolonged prodromal stage supports this theory, as the outflow of fluid shows a tendency to compensation for the increased supply, until finally the outlets are obstructed. It is also possible that congenital changes in the outlets may likewise play a part, although this question must remain open, in view of the almost complete lack of anatomic studies on eyes with juvenile glaucoma (Smith[21]).

The effect of Graefe's iridectomy, according to Fortin,[22] "depends on the opening of the iridociliary chamber, whereby the outflow of its contents toward the canal of Schlemm is facilitated." This explains the conditional value of the operation in cases of glaucoma. To the facilitation of the outflow may be added the removal by iridectomy of a small portion of the iris and by excision of the ciliary body (cyclectomy[23]), or its obliteration by electrolysis, of a larger portion of the glaucomatous uvea, with its increased secretion of fluid due to the hyperactivity of the psychoreflex. These operations cannot, however, be regarded as reliable, for the obliteration of the outlets of the eye is a progressive process, and arrest can be expected only in exceptional cases. As a matter of fact, sooner or later—sometimes only after many years—progressive obliteration leads to new obstruction. This explains the futility in particular of iridectomy treatment of simple glaucoma; in the two other forms of the disease the correspondingly greater reduction in secretion of fluid will for a long time compensate for the obliteration of the outlets. Cyclodialysis, on the other hand, is directed against the obstruction itself. Of course if the patient with glaucoma dies before return of the tension, the case is classified in the statistics as one of successful operation. The superiority of the filtrating operations, especially iridotorsion, is thus self explanatory.

20. Löhlein, W.: Arch. f. Ophth. **85**:393, 1913.
21. Smith, P.: Ophth. Rev. **13**:215, 1894.
22. Fortin, E. P.: Semana méd. **2**:207, 1939.
23. Denig, R.: Iridotorsion, Iridectomy and Cyclectomy. Arch. Ophth. **31**: 242 (March) 1944.

12. From the preceding discussion, it is clear that animals, owing to their primitive psychogenic endowment, are exempt not only from sympathetic ophthalmia and sympathetic irritation but from primary glaucoma. In fact, both Schleich[10] and Nicolas[24] asserted that hitherto the condition known in man as simple glaucoma or inflammatory glaucoma without enlargement of the eye and without hydrophthalmos, has not been observed in animals. Fully developed glaucoma in animals occurs exclusively in the form of hydrophthalmos due to hereditary inhibition of development, as in the case of congenital hydrophthalmos in man.

POSSIBILITIES OF PSYCHOTHERAPY

The significance of the psyche in the development of sympathetic ophthalmia and glaucoma suggests the possibility of their vasomotor and sensory control by psychotherapy. A blister resembling that due to burn can be induced by hypnosis or can be prevented in cases in which it would naturally appear. Likewise, a menstrual hemorrhage can be induced or checked, and hyperesthesia can be transformed to anesthesia. It seems plausible therefore, especially in cases of laceration of the uvea, to attempt hypnotic treatment simultaneously with the usual methods of treatment (Gill[25]), in an attempt to prevent metastasis. However, one must decide in the particular case whether this is advisable in the presence of a greatly damaged uvea with continued severe irritation, so that one may not miss the right moment for enucleation. The indications for enucleation and isolation remain the same whether or not hypnotic treatment is employed. In the presence of primary glaucoma with progressive changes in the eye hypnotic treatment could hardly be considered. To what extent already developed sympathetic ophthalmia might be influenced thereby cannot be stated.

56 East Fifty-Eighth Street.

24. Nicolas, E.: Ophtalmologie vétérinaire et comparée. Paris, Vigot Frères, 1928.
25. Gill, W.: South. M. J. **34**:959, 1941.

IRIDOTORSION; IRIDECTOMY; CYCLECTOMY

RUDOLF DENIG, M.D.

NEW YORK

Greenwood's [1] method of incising the iris on both sides of the iris forceps is equivalent to an isolation procedure, such as I recommended in 1927 for old, inflammatory prolapse and incarceration of the iris with danger of sympathetic ophthalmia. The segment of iris not only is thereby cut off from its connection with the rest of the iris, losing its wick effect, but constitutes a useless and nonvital, and under certain circumstances even dangerous, flap. Owing to its shortness, it may slip back, an occurrence which Greenwood tried to prevent by instillation of atropine, thus risking obstruction of the scleral hole and a lighting up of the glaucomatous process. The lowering of tension obtained by Greenwood is attributable to the simultaneously performed sclerectomy, so that in the final analysis his procedure consists of a Lagrange operation, rendered only more complicated and dangerous by his alleged improvement.

Fortin,[2] at the Fourth Brazilian Ophthalmological Congress, held at Rio de Janeiro, Brazil, in June 1941, expressed a similar opinion, extolling as a special advantage of iridotorsion the embedding of living iris tissue in a canal, which favors filtration, instead of the formation of a nonvital fistula (fistula inerta).

As iridotorsion was evolved from the isolation procedure by retrograde deduction, the paradox of a two sided incision of the iris is clear. When the iris is incised on one side only, it is maintained in vital connection with its trunk, while at the same time its length is doubled. The latter provision prevents its sliding back and renders possible the formation of a cushion to close the scleral hole.

The purpose of cutting only one iris pillar is not only to supply such a cushion, as an insurance against late infection, but, primarily, to permit a free passage of intraocular fluid into the subconjunctival space. For this reason, the segment of iris must be protected from any form of incarceration. This prerequisite condemns as unreliable, and even dangerous, all operations for incarceration, such as that of Holth, and their modifications.

Accordingly, iridotorsion should aim at establishment of a perfect sclerectomy channel, for this constitutes the tube into which the sensitive iris wick, so easily rendered impermeable by pressure, is to be embedded. The success of the operation will depend primarily on the meticulous execution of this step. As the technic of iridotorsion has already been described,[3] I shall discuss here only certain important details.

A more lateral incision is to be considered only if later removal of a coincident cataract is planned. Ordinarily, the incision in each eye is placed between 10:30 and 1:30 o'clock, the conjunctival flap, on the other hand, being between 10:30 and 2 o'clock in the right eye and between 1:30 and 10 o'clock in the left eye. Whereas formation of the flap in both eyes begins on the temporal side, right at the limbus, it ends on the nasal side 3 to 4 mm. from the limbus and somewhat farther down.

The puncture is made with the Graefe knife 1 mm. from the limbus, just outside the conjunctival flap, and the counterpuncture likewise 1 mm. from the limbus, with the flap turned down. The distance from the limbus of the sites of puncture and counterpuncture may be judged by the surgeon, as in the presence of a narrow anterior chamber they may have to be made in the cornea, but for the completion of the incision, i. e., at 1 mm. from the limbus at 12 o'clock, a guide mark of india ink is imperative. On its way upward, the knife must glide close along the surface and the root of the iris, must be kept 1 mm. distant from the limbus and must not be permitted to enter the superficial layers of the sclera, as the spur which is to be formed must include the entire thickness of the sclera. Otherwise, only the surface of the sclerectomy opening, and not its base, will measure 1 mm. in width. To serve as a guide for the knife on its upward course, with a moistened strabismus hook, the tiniest dot of india ink is placed on the

1. Greenwood, A.: Comparison of Operations for Chronic Glaucoma, Arch. Ophth. **10**:472 (Oct.) 1933.

2. Fortin, E. P.: Tratamientos de las afecciones glaumatosas, Arch. de oftal. de Buenos Aires **16**:316, 1941.

3. Denig, R.: Iridotorsion: Confirmation of Its Anatomic Basis by Fortin's Investigations on Glaucoma, Arch. Ophth. **24**:482 (Sept.) 1940.

sclera at 12 o'clock at a distance 1 mm. from the limbus, as any other mark runs the risk of being made invisible by pressure of the knife on the tissues during the section. With the same hook, the ink is branded into the superficial layers. Then, in order to be certain of the distance of 1 mm., the surgeon measures the distance once more.

A scleral hole of 1 mm. suffices perfectly for the embedding of the iris wick, provided that, as already mentioned, its base—and everything depends on this—has a width of 1 mm. Since the ciliary body begins 1.5 mm. from the limbus, the danger of its prolapse, or a prolapse of the vitreous, is no greater than the risk in the case of iridectomy for glaucoma. This should encourage even the most timid operator to keep his knife under the scleral spur until it has reached the level of the ink spot. Only by obeying this rule may he count on getting a satisfactory scleral channel. Without this ink mark he is groping in the dark. The reason for this is that the divergent forces exerted by the upward advancing knife and the opposing fixation forceps, at 6 o'clock, elongate or stretch the eyeball, this effect being especially favored by increased edematous saturation of the sclera in cases of acute and chronic glaucoma. For when the knife passes the region of the limbus at 12 o'clock, it would often seem already to have advanced beyond the 1 mm. point if the ink spot did not serve as a "beacon" to correct this impression.

Of great aid to the surgeon in guiding the incision is the placing of a bridle suture. This is inserted on the nasal side at 3 or 9 o'clock, either in the corneoscleral region or in the tendon of the internal rectus muscle. Without the bridal suture, owing to the shortness of the incision and the rigidity of the limbus resulting from the glaucoma, the advancing knife may meet with such opposition that, quite aside from the danger of evulsion of the conjunctiva at the site of fixation at 6 o'clock, the course of the incision may be rendered uncertain by deviation of the eyeball. Furthermore, the procedure may be slowed up, the delay entailing the escape of aqueous. All these inconveniences may be averted by employment of the bridle suture. This suture likewise renders possible a better arrangement of the assistant's duties. He not only takes charge of the bridle suture but maintains fixation of the eyeball at 6 o'clock. The surgeon, on the other hand, attends to the conjunctival flap. He seizes it with his left hand with an anatomic forceps and draws it down over the cornea, shortly before the counterpuncture is made, then withdraws it a little to permit visual control of the upward gliding knife and finally brings it down again.

Owing to the shortness of the incision and the danger of injury to the capsule of the lens, an iris hook is preferable to an iris forceps for pulling out the iris. Once the iris is drawn out, it is seized with the iris forceps, held in the left hand, and drawn tense, and then the right pillar is cut off with the de Wecker scissors, which are held in readiness in the palm of the right hand. Both in the right and in the left eye, the right pillar should be cut, for reasons of handedness.

Before the iris is wrapped about a hairpin-thin dental probe (torsion), it is advisable to prepare the flap suture; as a rule, one such suture will suffice. For this purpose, the threads are brought through the edge of the flap and the scleral conjunctiva and tied, with a loose loop, when torsion has been completed. In this way, the danger of disturbance of the iris cushion is reduced to a minimum.

Iridotorsion demands accurate observance of all these details, but the care repays the surgeon with results far superior to those of any other operation for glaucoma.

The relation of iridotorsion, cyclodialysis and iridectomy to each other is illustrated by the following case.

Mrs. K. de L., aged 46, had suffered for two years from simple glaucoma of both eyes. For a long time the tension was kept below the 25 mm. limit by two daily instillations of a 2 per cent solution of pilocarpine. Recently, however, an increase of tension had been noted in the right eye. Tension was 32 mm. in this eye and 24 mm. in the left eye. Vision and the visual fields were intact in both eyes.

On Dec. 26, 1939 iridotorsion was successfully performed on the right eye. As a rise of tension in the left eye could be only a matter of time, the patient was advised two weeks later to undergo iridotorsion on the other eye, but she refused. At the end of January 1941 the expected symptoms developed in the left eye. The tension had increased to 30 mm., and vision had diminished to 20/30, with the occasional appearance of rainbows.

In the meantime, however, the anterior chamber had become so shallow that iridotorsion could no longer be contemplated. For this reason, on January 27, an outward and downward cyclodialysis was performed. The patient was previously told that this operation would be only preliminary and that iridotorsion would be required as soon as the irritation had subsided somewhat. Immediately after cyclodialysis, the patient being still on the operating table, the anterior chamber deepened, and three days later the tension fell below normal, so that an early iridotorsion could be planned. During the night of February 3-4 an acute attack of glaucoma developed, with intolerable pain and extreme edema of the conjunctiva and the upper eyelid. The tension was 3 plus. Vision was reduced to perception of hand movements. Fortunately, the anterior chamber was

still deep enough to permit performance of iridotorsion, with the patient under general anesthesia. The operation proved to be successful, vision eventually being restored to 20/30.

This case shows (1) that no great reliance can be placed on cyclodialysis; (2) that it is advisable to perform cyclodialysis and iridotorsion at one sitting, provided the anterior chamber deepens immediately after cyclodialysis, and (3) that with a scleral spur as narrow as 1 mm., iridotorsion can be performed instead of the Graefe iridectomy, even in cases of acute glaucoma, and is more reliable.

If, however, the anterior chamber should not deepen sufficiently after cyclodialysis to permit introduction of the Graefe knife, preliminary posterior sclerotomy or cyclectomy might be considered. My experience with the former procedure has not been encouraging. The latter operation is performed in cases of traumatic prolapse of the ciliary body but has not yet been employed in cases of glaucoma.

CYCLECTOMY

Prolapse of the ciliary body, with subsequent iridocyclitis and atrophy of the eye, has been observed in the course of Lagrange's operation. In the cases of iridotorsion which I have performed, I have never seen prolapse of the ciliary body. Such good results are attributable solely to care in keeping the base of the sclerectomy opening 1 mm. in width. If such a prolapse should occur, however, I should not hesitate a moment to perform an excision.

The chief prerequisite for success is care not to leave even the tiniest shred of uveal tissue between the edges of the wound. In this connection, I refer to my article appearing in this issue of the ARCHIVES.[4]

I performed cyclectomy in 2 cases of absolute glaucoma, in 1 of which the iris was atrophic. The ciliary body prolapsed immediately into the wound and could easily be drawn out, but the iris could be removed only in shreds. For this reason, I decided to do an immediate enucleation. It would probably have been better to have left the friable iris in situ and to have been content with a cyclectomy; perhaps, too, instead of use of the forceps, the introduction of a blunt iris hook, after previous puncture of the pectinate ligament with the spatula, might have made possible delivery of the iris intact.

In the other case, cyclectomy yielded a splendid coloboma of the ciliary body and iris. Examination of the blind eyeball, removed for suspected tumor on the basis of a diagnosis made elsewhere, showed that the coloboma had smooth edges. Near the ora serrata there remained a ridge, scarcely 1 mm. in width, as a bridge between extensions of the ciliary processes. The incision was 2.5 mm. from the limbus, and parallel with it, and was 6 mm. long. At first the ciliary body seemed reluctant to come out. For this reason one scleral lip was drawn downward with a sharp hook. In both cases the operation was complicated by slight loss of vitreous. Subluxation of the cataractous lens did not occur.

Of course it is not possible at this time to offer any final evaluation of cyclectomy. It can be stated, however, that the procedure should be kept in mind as a possibility.

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4. Denig, R.: Prolapse of the Uvea: Treatment and Significance in Interpretation of Sympathetic Ophthalmia and Glaucoma, Arch. Ophth., this issue, p. 232.

MENINGOCOCCIC CONJUNCTIVITIS

CAPTAIN FREDERICK H. THEODORE
MEDICAL CORPS, ARMY OF THE UNITED STATES
AND
CAPTAIN PAUL F. KOST
SANITARY CORPS, ARMY OF THE UNITED STATES

The purpose of this communication is to call attention to the frequency of meningococcic conjunctivitis during periods in which the incidence of meningococcemia and of meningococcic meningitis is high and to emphasize the importance of routine bacteriologic examination of the conjunctival discharge in all cases of acute catarrhal conjunctivitis encountered, particularly at such times. The cases described in this report occurred during a period in which both clinically and on the basis of laboratory investigations it was apparent that such conditions existed. Neisseria intracellularis may occasionally be recovered from the normal conjunctiva of carriers, as well as from the nasopharynx.[1] The occasional occurrence of meningococcic conjunctivitis in the course of the first, or "carrier," stage of cerebrospinal fever is well known.[2] Sometimes the infection of the conjunctiva appears to be endogenous, occurring simultaneously with bacteremia.[3] Here, too, the organism may be recovered from the conjunctiva. In such cases the patient is ill and shows signs of toxicity. It may be necessary to emphasize, however, that perhaps in most cases of meningococcic conjunctivitis the ocular infection should be described as extrameningeal, occurring as a pure conjunctival infection which may subside under nonspecific therapy, or may even be self limited. In cases of this type there are otherwise no symptoms, or at most mild nasopharyngitis, not uncommon in cases of acute catarrhal conjunctivitis. Unless the case is complicated by other conditions, the patient is afebrile. The incidence of this type of localized extrameningeal infection may be ascribed to the increase of droplet infection accompanying living conditions, altered by climatic factors, such as a drop in temperature, and to the relatively high resistance of the host.

The early recognition of meningococcic conjunctivitis is of great importance, for two reasons: First, in cases in which the infection may go on to meningococcemia and meningitis, the great value of early administration of sulfonamide compounds is obvious. If treatment is started early enough, the mortality rates are exceedingly low. Even a few hours may make a decided difference. Second, even if the infection remains limited to the eye and it responds to local treatment, it is of the greatest importance to prevent the patient from becoming a carrier. To this end, he must be hospitalized and given sulfonamide compounds for a time, perhaps a week or two.[4] With the increased, and almost routine, use of ophthalmic sulfonamide ointments, the conjunctivitis may soon clear up clinically, but the patient may become a source of infection, unless he is given general chemotherapy.

Clinically, one cannot distinguish the conjunctivitis due to N. intracellularis from other types of severe catarrhal conjunctivitis, although one may suspect it when the known incidence of this infection is high. At such times a particularly profuse mucopurulent discharge, rapidly reappearing after the eye is cleansed, associated with a greatly inflamed and edematous conjunctiva and swelling of the lids, may suggest the cause. Subconjunctival hemorrhages may be present, as well as preauricular lymphadenopathy. However, severe acute pneumococcic or staphylococcic conjunctivitis can give exactly the same appearance. In our cases the cornea was not involved. A less hyperacute type of conjunctival reaction may also occur. Usually only one eye is affected, although of course both can be.

The diagnosis therefore depends entirely on bacteriologic methods. In the 8 cases to be described in this paper the diagnosis was made only because it was routine policy to study smears of secretions stained by the Gram method in all cases of acute catarrhal conjunctivitis. Whenever possible, the slide was examined before the

From the Station Hospital, Miami Beach Training Base Army Air Forces Technical Training Command, Miami Beach, Fla.

1. Duke-Elder, W. S.: Textbook of Ophthalmology, St Louis, C. V. Mosby Company, 1938, vol. 2, p. 1535.
2. Cecil, R. L.: A Textbook of Medicine, ed. 5, Philadelphia, W. B. Saunders Company, 1940, p. 214.
3. Duke-Elder,[1] p. 1547.
4. Feldman, H.: Personal communication to the authors.

patient left the clinic. Epithelial scrapings, stained by the Giemsa method, were generally also made for special studies. When Gram-negative diplococci were seen, the patient was immediately sent to the laboratory for a confirmatory smear and culture and was then hospitalized. In cases of acute conjunctivitis diagnosis on the basis of the smear is often more valuable than dependence solely on cultural methods. This is particularly true when one is dealing with as delicate an organism as the meningococcus. Moreover, a positive smear in a case of meningococcic conjunctivitis is loaded with the organisms, in contradistinction to the relative paucity of the specific organisms in cases of equally severe conjunctivitis due to pneumococci or staphylococci. As it was possible to rule out gonorrhea in each of our cases, and as the infections were milder than the process seen in cases of gonococcic conjunctivitis, the diagnosis was easily made before culture.

TECHNIC OF CULTURE

Cultures of nasopharyngeal material were made in some of the cases but did not yield meningococci. It is possible that such cultures might have been positive had the patients gone untreated for longer periods. Blood cultures were not made, as none of the patients appeared sick enough to warrant such studies.

The material for culture was taken from the eye with a swab dipped in 1 per cent tryptose broth. The swab was then streaked on a proteose 3–hemoglobin plate in such a manner that a considerable portion of the plate gave well isolated colonies, which could be easily examined and evaluated. The colony produced on this medium is clear and transparent at the periphery and tends to become slightly gray near the center.

A direct smear was always made at the same time that material for culture was taken. This smear was stained by the Gram method and examined for organisms of the morphologic character and reaction to Gram's stain of N. intracellularis.

The plate was incubated at a temperature of 37 C., under approximately 3 per cent carbon dioxide tension, obtained by means of a candle jar. After twenty-four hours the plate was examined, and typical colonies were picked and transferred to slants of proteose 3–hemoglobin agar. In some cases the colonies were so numerous that identification could proceed directly from the plate.

Pure cultures of typical organisms from the plate were inoculated into tubes of dextrose, maltose and sucrose broth. Positive reactions could often be noted in four or five hours, as N. intracellularis causes formation of acid in dextrose and maltose broth and does not produce fermentation of sucrose broth. Since our broths contain 0.1 per cent agar, the first signs of fermentation take place at the surface.

At the same time that broth cultures were set up, we checked the agglutination reaction of the organism in polyvalent antimeningococcic serum. In the last 2 cases reported we were also able to obtain the type-specific anti-serums I, II and IIa. With use of the aforementioned methods, we were able to identify the organism morphologically, chemically and serologically.

TREATMENT

All the patients were given sulfonamide compounds, both locally and orally. In most cases 5 per cent sulfathiazole or 5 per cent sulfadiazine was used as an ophthalmic ointment and was applied every three hours. In some cases 5 per cent sulfanilamide ointment was also used effectively. In addition, sulfadiazine was administered orally—1 to 2 Gm. three times a day. In less than forty-eight hours, generally in twenty-four hours, the discharge became minimal, if not absent. Smears taken in several cases at this time revealed no organisms. Every patient was completely well in five days, the conjunctiva revealing no injection. There were no corneal complications. Oral administration of sulfadiazine was generally stopped after five days, although it might have been better to keep up the treatment for another week, to be sure that the patient was free from N. intracellularis.

REPORT OF CASES

All the patients, with 1 exception, were first seen at the Ophthalmic Clinic, Station Hospital, Miami Beach Training Base, and then hospitalized in unit 2, the contagion unit of the Station Hospital, under the care of Major James W. Britton, of the Medical Corps.

CASE 1.—This case will be described and discussed in more detail than the others. K. W. S. was first seen on Jan. 27, 1943, because of severe acute catarrhal conjunctivitis in the left eye, which had been present three days. Routine treatment, consisting of local application of a 1 per cent solution of silver nitrate and the home use of drops of 0.25 per cent zinc sulfate and a 5 per cent sulfathiazole ointment was instituted after a smear of the conjunctival discharge had been made. Owing to difficulties, the smear was not examined until the patient's second visit, two days later, at which time the discharge had increased considerably and a good deal of chemosis had appeared. The cornea was normal. Examination of the old, as well as of a fresh, smear revealed many Gram-negative extracellular and intracellular diplococci, and it was erroneously concluded, therefore, that he had gonococcic conjunctivitis of relatively mild severity, despite the absence of evidence of urethritis. Cultures, unfortunately, did not yield the meningococcus.

The patient was immediately hospitalized. Treatment consisted of the oral administration of 4 Gm. of sulfathiazole daily and the almost constant use of 5 per cent ophthalmic sulfathiazole ointment locally. A decided improvement was soon noted, and after thirty-six hours a smear of the remaining minimal secretion was negative for meningococci. All conjunctival injection disappeared within three days, and the patient was discharged as cured six days after admission. Except for his eye, he had been otherwise well.

Because of the increased number of cases of meningococcic infections of all types that appeared at this time, including a number of cases similar to this one, to be described, in which cultures were positive for meningococci, there can be little doubt that the condition in this case had a similar cause.

Moreover, it was learned that the patient had not used the sulfathiazole ointment furnished him more than

once or twice before his admission, so that he probably presented an excellent example of a pure extrameningeal meningococcic infection which remained localized, although untreated, in this case for five days.

CASE 2.—B. T. was seen on Feb. 15, 1943, with bilateral acute catarrhal conjunctivitis of two days' duration. He also had acute nasopharyngitis and bronchitis. The latter condition, together with the clinical resemblance to the condition in case 1 and the absence of known exposure to gonorrhea, suggested meningococcic infection, a diagnosis which was confirmed by the presence of gram-negative intracellular diplococci on the smear. Cultures showed no growth.

He was immediately hospitalized and treated with 6 Gm. of sulfadiazine daily and local applications of 5 per cent ophthalmic sulfanilamide ointment. After two days the discharge had completely subsided, and the dose of sulfadiazine was reduced to 3 Gm. daily. A smear of the conjunctival secretion made one day after admission revealed no organisms. He was discharged as cured six days after admission.

CASE 3.—S. M. McC. had had a severe head cold for five days prior to admission, on Feb. 24, 1943, because of severe catarrhal conjunctivitis in the left eye, which had appeared the night before. He still had nasopharyngitis. Gram-negative intracellular diplococci were present on smears of the conjunctival discharge, and in this case cultures were positive, revealing similar organisms which agglutinated with polyvalent antimeningococcic serum. Specific typing could not be carried out.

Because of the positive smear, the patient was immediately hospitalized and treated with 3 Gm. of sulfadiazine daily. No local treatment was given. In three days his eye showed great improvement, and by March 2 it was well. Treatment was discontinued on March 3, and he was discharged on March 9.

CASE 4.—G. M. S. was seen on March 25, 1943, because of severe catarrhal conjunctivitis in the left eye, which had developed overnight. Immediate examination of a smear of the secretion revealed the characteristic organisms, and gram-negative diplococci, which agglutinated with polyvalent antimeningococcic serum were grown on culture. The patient had a temperature of 101.8 F., which was probably due to rubella, as he had a macular rash typical of this condition. He was the only patient to have fever.

He was hospitalized and given 6 Gm. of sulfadiazine daily by mouth and 5 per cent ophthalmic sulfadiazine ointment locally. His fever was gone in two days. The conjunctivitis greatly improved in two days and had disappeared by the sixth day. The oral dose of sulfadiazine was reduced to 3 Gm. daily at the end of two days and was stopped altogether after four days.

CASE 5.—R. W. O'N. was seen April 12, 1943, with particularly hyperacute conjunctivitis in the right eye, of one day's duration. There was severe chemosis. Smears were loaded with gram-negative intracellular diplococci, and the diagnosis was later confirmed by the culture of similar organisms, which gave characteristic sugar reactions. Typing, done elsewhere, was reported to reveal type I. Culture of material from the nasopharynx obtained when the patient was first seen gave no growth.

The patient was hospitalized and treated for seven days with 3 Gm. of sulfadiazine daily and local applications of 5 per cent ophthalmic sulfanilamide ointment. The usual quick response to treatment followed in a few days. He was kept in the hospital for a longer period, however, as both his eyes later became moderately injected. This proved to be due to the limbic form of vernal catarrh. Epithelial scrapings taken at this time and stained by the Giemsa method revealed huge numbers of eosinophils, but no bacteria.

CASE 6.—A. A. was also seen on April 12, 1943, because of moderately severe acute catarrhal conjunctivitis in the right eye, of only eight hours' duration. A smear revealed gram-negative intracellular diplococci, but cultures of secretion from the conjunctiva did not yield organisms, while the culture of material from the nasopharynx showed no typical organisms. Treatment was similar to that in case 5, and within twelve hours notable improvement was seen. General treatment was discontinued in five days. His eye had cleared up completely in three days. Nothing was found to indicate any cause other than meningococcic infection.

CASE 7.—J. M. was first seen May 21, 1943 for severe acute catarrhal conjunctivitis in the right eye, of one day's duration. Many gram-negative diplococci were observed in a smear, and cultures yielded similar organisms, which agglutinated with both polyvalent and type I antimeningococcic serum. The treatment and course were similar to those in the other cases.

CASE 8.—R. R. M. was seen in consultation at the convalescent unit of the Station Hospital on March 30, 1943, where he was under treatment for an ailment of the knee. Moderately acute catarrhal conjunctivitis had developed in the left eye the day before. Culture revealed a few gram-negative diplococci, which agglutinated with polyvalent antimeningococcic serum. Local treatment with 5 per cent ophthalmic sulfathiazole ointment was alone used, and the next day the eye appeared practically healed.

Clinically, the bacteriologic report was a great surprise, but there was no question of its validity.

SUMMARY

The incidence of extrameningeal infections increases at times when meningococcic meningitis is prevalent. Apparently, the conjunctiva is a common site of extrameningeal involvement. In the 8 cases of meningococcic conjunctivitis presented here, with laboratory data, the diagnosis was made only as a result of the routine examination of smears of secretion in all cases of acute catarrhal conjunctivitis encountered. The importance of the recognition of this type of conjunctivitis is twofold: First, it may be the first stage of meningococcic meningitis, and, second, even if the process remains localized to the eyes and is cured by nonspecific, routine measures, the patient may become a carrier of the organisms.

RHINOCANALICULAR ANASTOMOSIS WITH RECONSTRUCTION OF THE LACRIMAL SAC

LOUIS BLUMENFELD, M.D.
BROOKLYN

The anatomy and physiology of the lacrimal system need not be reviewed, as they are both well understood.

Among the better known operative procedures on the lacrimal drainage system are those of West, Toti, Mosher and Halle. The results of these operations have often been disappointing, owing to the fact that they use as part of their reconstructive tissue a lacrimal sac that is chronically diseased, fibrotic, the site of strictures and often in the stage of active suppuration. The intranasal operation of Halle is difficult to perform because of a limited visual field. These operations usually require a course of postoperative probing and irrigation in order to obtain a functioning system. Often in spite of all such treatment epiphora has persisted.

The operation presented here is, to my knowledge, original with me. In a careful review of the literature I could find no account of a similar operation. The result obtained in the case reported here was immediate and gratifying. The patient was discharged with a normally functioning lacrimal system within two weeks after operation. No probing was done, either before or after operation. I believe none will be necessary. Epiphora over the face and through fistulous openings on the side of the nose was eradicated, and normal lacrimal drainage was instituted. I believe that no scars or strictures will form, since the tears have a continuous channel lined with normal epithelial tissue.

REPORT OF A CASE

History.—C. R., a white woman aged 32, had a history of abscess under her right eye at the age of 8 months. The abscess was opened by a physician. The eye began to tear over her face. When her mother pressed the corner of the eye, it filled with pus. This condition continued until she was 17 years of age, when a second operation was performed. The physician said he removed the tear sac. The wound did not heal and continued to discharge pus. She was again operated on by the same surgeon. Again, the wound failed to heal, and pus continued to discharge through a sinus in the side of the nose. A fourth operation was done. This time the physician said "he scraped the bone and removed as much granulation tissue as he dared, without ruining her face." After the last operation the cutaneous wound healed, but the eye continued to tear not only over the face but from two holes on the side of the nose. This condition persisted for fifteen years (up to the time I saw her).

The patient came to my office seeking relief from both the epiphora and the fistulous openings on the side of the nose.

Examination.—The skin over the site of the right lacrimal sac was firmly adherent to the nasal wall. Tears were flowing from two small openings in the side of the nose about ¼ inch (0.5 cm.) from the inner canthus. These fistulas were the distal openings of the upper and lower canaliculi. The patient consulted several ophthalmic surgeons, who advised her having the canaliculi slit open and curetted and the puncta cauterized so that the fistulous openings would clear up. They stated that the epiphora would continue. In her opinion, the results to be obtained did not warrant such a procedure.

After careful examination and study of the canaliculi and nasal structures, I informed the patient that I believed I could reconstruct the lacrimal drainage system so that it would function normally, and not only eradicate the fistulous openings on the side of the nose but eliminate the epiphora over the cheek.

Operation.—In this procedure the tissues are anesthetized with a 2 per cent solution of procaine hydrochloride and epinephrine hydrochloride (1:1,000). A curved incision is made between the fistulous openings and the nasal wall. The skin is carefully dissected free down to the canalicular openings. A countercurved incision is now made between the openings and the inner canthus to complete an oval with the first incision. The skin around this incision is also carefully dissected for a short distance toward the fistulas. This oval flap of skin, with the canaliculi attached, is to form the upper part of the reconstructed lacrimal sac. It is important that the flap be carefully planned and protected until the operation is completed.

The subcutaneous tissue and the periosteum of the nasal wall are now elevated, with exposure of portions of the nasal bone and the frontal process of the superior maxilla. A fair-sized, vertically oval window is made into these bones of the lateral nasal wall. The window is situated just anterior to the anterior tip of the middle turbinate. The nasal mucous membrane is thus exposed. This membrane is undermined for a few millimeters around the oval window. A vertical incision is made in the nasal mucous membrane, so that the nasal chamber is entered just anterior to the anterior tip of the middle turbinate.

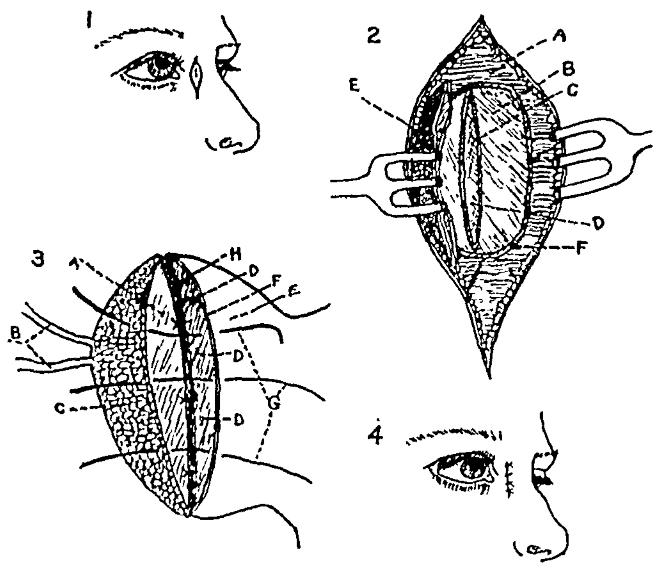
The oval cutaneous flap, containing the canalicular openings, is now carefully approximated, without tension, to the incised margins of the nasal mucous membrane. The posterior lip of the incised mucous membrane is carefully sutured to the inferior lip of the oval cutaneous flap. The anterior lip of the mucous

membrane is sutured to the upper lip of the cutaneous flap, a new lacrimal sac, with two canalicular openings anteriorly and a large nasal opening into the nasal chamber being thus created. The edges of the cutaneous incision are now carefully approximated over the newly reconstructed lacrimal sac; this completes the operation.

In the present case the canaliculi were not probed or irrigated. In forty-eight hours mild protein silver was drained freely into the nasal chamber. The external cutaneous sutures were removed on the fourth day.

COMMENT

In view of the fact that this operation was not difficult and the results were so immediate and gratifying, it occurs to me that in cases of chronic suppurative dacryocystitis in which the sac is destroyed by infection and scarring, or has even been removed, so that the patient has more or less permanent epiphora, it would be not only a proper measure, but even the procedure of choice, to establish fistulas of the lacrimal canaliculi on an elected site on the nasal wall as a preliminary step. This operation is to be followed by a period of waiting for the fistulas to establish free drainage; if necessary, this drainage should be aided by occasional probing and irrigation. The procedure should be simple, since both the puncta and the artificially created fistulas are on the surface of the skin and are both amenable to treatment under direct visualization. Then, after a suitable period of waiting, the aforedescribed operation should be performed.



1, oval incision in the skin surrounding fistulous openings of the upper and lower canaliculi.

2, a close-up view of the operative detail in the nasal wall. *A*, is the lateral nasal wall, in which a vertically oval window has been made; *B*, the nasal mucous membrane; *C*, an incision in the nasal mucous membrane; *D*, the nasal chamber anterior to the anterior tip of the middle turbinate; *E*, the oval cutaneous flap retracted to one side, and *F*, the frontal process of the superior maxilla.

3, detail of reconstruction of the lacrimal sac and its implantation into the nasal chamber. *A*, indicates the oval flap of skin turned in so that the epidermal surface faces the opening into the nasal mucous membrane; *B*, the upper and lower canaliculi; *C*, the subcutaneous surface of the cutaneous flap; *D*, the opening into the nasal mucous membrane; *E*, the nasal mucous membrane; *F*, the incised nasal mucous membrane; *G*, placing of the sutures, with closure of the reconstructed lacrimal sac, and *H*, the nasal mucous membrane and the cutaneous flap in close approximation, with sutures already placed and tied.

4, appearance of the cutaneous suture after completion of the operation.

This procedure eliminates most of the undesirable features of other operations on the lacrimal system. Both ends of the canaliculi can be probed, dilated and irrigated under direct visualization, so that the chances of the mucous membrane of the canaliculi being torn, with resultant scarring and strictures, are minimized. Diseased mucous membrane of the lacrimal sac is not used, as it is in the West, Toti and Halle operations. One does not go through an area that has previously been infected and scarred. There is always the possibility of reinfection from the nasolacrimal duct. Healthy normal tissues are used throughout the entire reconstructed lacrimal system, so that the danger of granulation and strictures is minimized.

CONCLUSIONS

Surgical treatment of the lacrimal drainage system has not kept pace with the progressive advancement in surgical technic as have other ophthalmologic and rhinologic procedures. Previous operations on the lacrimal system were often followed by more or less permanent epiphora, a condition which required postoperative probing and irrigation. The operation described here provides the patient with a new sac and a large nasal opening, all made of normal tissue. No postoperative manipulations have been necessary.

With the technic described, a patient suffering from chronic suppurative dacryocystitis can be promised not only relief from an infection that is potentially dangerous to the eye but a normally functioning lacrimal drainage system, without epiphora.

221 Brooklyn Avenue.

CATARACT PRODUCED BY ANOXIA

JOHN BELLOWS, M.D., PH.D., AND DOROTHY NELSON, PH.D.
CHICAGO

The transparency of the crystalline lens depends on the proper utilization of nutrient material supplied by the aqueous. If for any reason there is a local deficiency of some vital constituent, the lens becomes opaque. Cataract has been reported to result from severe inanition,[1] as well as acute thirst.[2] Curtis and co-workers [3] showed that mature cataract developed in rats maintained on a tryptophan-free diet within six to seven weeks. Recently Totter and Day [4] confirmed these reports. By deprivation of cystine, cataract is produced in larvae of the salamander.[5] It is possible that deficiencies in other essential amino acids will lead to cataract. Deficiency in riboflavin leads to cataract in rats.[6] While vitamin D deficiency in itself does not cause cataract, tetany, which is frequently associated with rickets, is often accompanied by opacities in the lens. For example, in some instances of cataract resulting from ligation of the posterior ciliary arteries [7] or the veins of the vortex [8] it is uncertain whether the opacities are the result of a deficient nutrient supply or the accumulation of waste products.

The most vital requirement of tissue is an adequate supply of oxygen. Tissues possessing a blood supply are bathed in a medium containing oxygen in a concentration of 13 to 19 volumes per cent. This large amount of oxygen is made possible by the hemoglobin of the red cells, which holds the oxygen in a loose chemical combination. The amount of oxygen in physical solution in the body fluids is extremely small. For example, the aqueous has only from 0.09 to 0.12 volume per cent.[9] The necessary rapid replenishment of oxygen in the aqueous is made possible by rapid diffusion from the ciliary body [10] and by the passage of oxygen from the atmosphere through the cornea.[11] In view of these facts, it is not surprising that lack of oxygen should have adverse effects on the lens, as our experiments have proved.

Biozzi [12] reported the effects of asphyxia on rats placed singly in 3 liter bell jars. He noted the evolution of cataract in some of these animals and subsequent regression of the opacity after a short time in the fresh air.

PRESENT INVESTIGATION

We undertook experiments to determine whether anoxia alone would produce cataract.

Fig. 1.—Cataract in eye of the rat produced by anoxia.

Rats were placed in a steel chamber in which the pressure was gradually reduced until it was equal to that at an altitude of 30,000 feet (9.1 kilometers) or more. When the conditions were severe enough so that 50 per cent of the animals died, it was found about 75 per cent of the dead animals and about 10 per cent of the survivors had opacities of the lens (fig. 1). That the

From the Departments of Ophthalmology and Physiology, Northwestern University Medical School.

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cataracts were due to anoxia and not to pressure was demonstrated by control experiments in which rats were placed singly in glass chambers arranged so as to permit the constant flow of a mixture of gases consisting of 5 per cent oxygen and 95 per cent nitrogen at a pressure equal to that at sea level. Again, the rats showed opacities in the lens, though to a lesser degree. / These bits, known to be resistant to changes in altitude, were employed. The aqueous was removed from one eye of each animal while the rabbit was under ether anesthesia. After recovery for two hours some of the animals were put in cages as controls; the others were placed in the decompression chamber. After two hours the pressure in the chamber was restored to a normal level;

Fig. 2.—Large oval vacuoles in the epithelial layer of the rat lens. High power magnification.

Fig. 3.—Section of cataract (rat) produced by anoxia, showing exudate on the capsule of the lens and clumps of epithelial nuclei.

experiments indicate that cataracts can develop during anoxia and that asphyxia and pressure are not important factors.

Since it is known that the oxidation of the lens is mainly anaerobic and that the lactic acid content of the aqueous is ordinarily higher than that of the blood, it was thought that a determination of the lactic acid content of the aqueous would be of interest. For this investigation rab-

the animals were anesthetized again, and the aqueous was removed from the second eye. The results were impressive. Whereas the average lactic acid content of the aqueous in all the eyes first studied and in the second eyes of the control rabbits ranged from 70 to 75 mg. per hundred cubic centimeters (a value somewhat higher than normal, probably the effect of the ether anesthesia), the average lactic acid content of

the aqueous in the second eyes of the animals in the decompression chamber was three to four times as high (250 mg. per hundred cubic centimeters). In order to determine whether the lenticular changes were due to a shift in the p_H of the aqueous, the pressure in the decompression chamber was reduced to that at an altitude of 30,000 feet. The p_H of the aqueous, removed under oil, was determined by the glass electrode method and was found to be unaltered. Therefore, the opacities were due either to a specific action of the lactic acid or, more likely, to an osmotic disturbance.[13]

Histologic Changes.—The difficulties in observation of microscopic changes corresponding to the opacities seen in living animals in experimental work is well known. However, the following changes were noted in some sections of cataract due to anoxia; vacuoles under epithelium (fig. 2), clumping of nuclei and exudate on the lenticular capsule (fig. 3). In cases of cataract produced by asphyxia Biozzi observed no changes in the capsule and epithelium, but in the cortex, 50 to 60 microns from the surface, he noted small vacuoles in rows, forming a layer 60 microns in thickness. In 2 lenses he described oval vacuoles parallel with the capsule, similar to those seen in cases of cataract due to anoxia.

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Ocular Changes.—After decompression there was conspicuous hyperemia of the iris. The beam of light in the aqueous, although difficult to observe, was visible. With oblique illumination small, diffuse, gray opacities were seen in the superficial part of the cortex. The most striking observation was the increased visibility of anterior superficial suture. With the higher magnification of the slit lamp, the changes were seen to begin with opacification of the anterior sutures, from which fine fibrillar opacities extended. In optical section it was seen that the entire opacity was thin and lay in the superficial layers of the cortex. Gradually the opacity extended peripheralward. Similar changes, although less conspicuous, occurred in the posterior portion of the cortex. In cases of extreme opacification the fiber structure was lost and a shiny white, total cataract was formed. The opacity lasted from about three quarters of an hour to one hour and then gradually regressed, the order of regression reversing exactly the course of development, so that the last opacities to disappear were those about the sutures.

Examination by one of us (J. B.) revealed no changes in the lenses of human volunteers placed in the decompression chamber and subjected to reduction in pressure to a level equivalent to that at an altitude of 18,000 feet (5.5 kilometers).

Northwestern University Medical School.

PSEUDOAPHAKIA FIBROSA

Report of a Case

MAJOR JOHN W. HARNED, MEDICAL CORPS, ARMY OF THE UNITED STATES

Congenital abnormalities of the lens present wide variations and are relatively common, but individual types of lenticular defects may be rare. Ida Mann has presented the most complete survey of developmental defects of the lens, and her description of secondary, or apparent, aphakia agrees well with the condition in the present case. The interest lies in the fact that neither eye is abnormal except for the lenticular defect.

. . . The lens is represented solely by a wrinkled capsule, often invaded and partially destroyed by vascular mesoderm, the resulting whitish membranous mass being supported in the pupil by ill-formed zonule fibers. The absorption and partial replacement of the lens by fibrous tissue opens up interesting speculations as to causation. One theory states that the lens develops normally but that its capsule is thinner than normal, and so ruptures, allowing of invasion by mesoblast and subsequent destruction of the lens. It seems more likely, however, that some primary fault in the lens fibers or temporary change in their environment causes them to degenerate and deliquesce. The capsule then shrinks and becomes opaque and more permeable, and the final reaction is the invasion by mesoblast in an attempt at repair.[1]

REPORT OF CASE

J. G., a boy aged 6 months, blond, the only child of Polish parents in Wisconsin, was of normal weight and had a normal skeletal development.

Family History.—The father, aged 30, was living and well. Examination showed no abnormalities. The mother, aged 27, was living and well but presented horizontal nystagmus and bilateral coloboma of the iris, extending from 7 to 5 o'clock. Needling operations on the lens had been performed in Milwaukee twenty-four years ago.

Personal History.—Since birth the child had failed to look directly at any object, and when he was a few weeks old nystagmus and convergent strabismus developed.

Physical Examination.—There were convergent strabismus of the right eye of approximately 30 degrees and slow horizontal nystagmus, with the quick component to the left. The pupils were small but reacted to light. The cornea of each eye was normal in size and both anterior chambers appeared deep, but the irises were not tremulous nor were colobomas present.

With induction of mydriasis a white, irregular plaque, 4 mm. in diameter, could be seen in the pupillary area, and fine strands were observed extending to the periphery. This plaque appeared as a white, irregular piece of paper would look if it were placed in the center of a spider's web. The fundus could not be seen except around the opaque area.

After a capsulotomy had been done on the left eye, at the age of 10 months, and on the right eye, at the age of 14 months, the entire fundus could be seen as a normal structure, and the capsular fibers retracted in a manner similar to that noted when the lens capsule is needled after cataract extraction. The white plaque offered the same resistance to the needle knife that is usually encountered in such a procedure.

CONCLUSION

In a case of pseudoaphakia fibrosa reported here the observations suggest that the defect was secondary aphakia, or pseudoaphakia, with degenerative changes occurring in the lens during the fifth week of embryonic life, as described by Mann, and not primary aphakia.

Norwegian American Hospital, Chicago.

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Clinical Notes

OPERATIVE TREATMENT OF PARALYSIS OF THE EXTERNAL RECTUS MUSCLE

H. MAXWELL LANGDON, M.D.; VAN MASHBURN ELLIS, M.D., AND ROBERT D. MULBERGER, M.D., PHILADELPHIA

Paralysis of an extraocular muscle from any source is difficult to overcome, and traumatic loss of power represents a most perplexing problem. Seldom can even a partial restoration of power be developed, and operative intervention is really the only hope. This means rearrangement of muscles and substitution of some other power plant for the one put out of action. In all probability the external rectus muscles offer the best field for this procedure, and we feel from our experience that loss of action of the external rectus muscle can be compensated for by operative intervention.

Two cases are reported here, in each of which outward rotation of the affected eye was completely lost and almost normal function was restored by transplantation of portions of the superior and inferior rectus muscles with recession of the internal rectus muscle and advancement of the external rectus muscle and Tenon's capsule.

REPORT OF CASES

In each case a child was injured in a motor accident, 1 at 6 years and 1 at 18 months of age. The older child had a partially developed fusion sense, which was disturbed and made almost useless by the accident, and the other child was injured so early in life that fusion sense and binocular vision had never developed.

In the first patient diplopia could be elicited in tests with a red glass, but no fusion could be developed with the rotoscope. The younger child had no diplopia.

CASE 1.—H. S., a white boy aged 9 years, was seen on Sept. 5, 1941, with a history of having been injured in a motor accident three years before. At that time he had been unconscious for seven weeks. On his return to consciousness it was found that his eyes were crossed and diplopia was present. The mother was told there was a fracture in the right frontal region of the skull. Examination showed normal vision in each eye, with the near point of accommodation at 10 cm. Motions of the right eye were normal. Diplopia involving the whole field of the left eye, typical of paralysis of the left external rectus muscle, was noted. No other ocular changes were observed.

On Nov. 17, 1941 the tissues around the outer portion of the eyeball, including the external rectus muscle, the conjunctiva and Tenon's capsule, were advanced; recession of the internal rectus muscle of 4 mm. was carried out, and the superior and inferior rectus muscles were split, the outer third of each muscle being sutured to the old attachment of the external rectus muscle and the tissues which had been advanced over them.

Healing was uneventful, and the 25 degrees of esotropia became 5 degrees of esophoria, with 8 degrees of hypertropia, as too much of the inferior rectus muscle had been transplanted to its new anchorage.

It was impossible to obtain fusion with the rotoscope, though the patient had binocular simultaneous vision The diplopia had disappeared.

He was last seen on Jan. 6, 1943, when there were normal vision, full outward rotation of the injured eye and no diplopia.

CASE 2.—H. McG., a girl aged 6 years, was injured in a motor accident at the age of 18 months, and after this the eyes, which had previously been straight, were converged, the left eye turning in.

Examination showed that vision was 6/9 in the right eye and 6/60 in the left eye. Rotations of the right eye were normal; those of the left eye were normal in all directions except outward, in which direction they were abolished. The eyes were healthy in all respects except for the absence of binocular vision.

Operative intervention was advised, and on Sept. 14, 1942 the left eye was subjected to the same proceeding as that followed in the first case, that is, recession of the internal rectus muscle; advancement of the paralyzed external rectus muscle and its covering, Tenon's capsule and the conjunctiva; splitting of the superior and inferior rectus muscles, and transplantation of the outer segments to the old attachment of the external rectus muscle.

Healing was uneventful, and on September 25 the patient was discharged, with good outward rotation.

She was last seen on Dec. 3, 1942. Vision was unchanged, with no fusion. The outward rotation of the right eye was 55 degrees, the upward rotation 30 degrees and the downward rotation 40 degrees.

Attempts to bring about recovery from loss of external rotation by damage to the sixth nerve have been made for many years, all of them being based on weakening of the internal rectus muscle of the affected eye and increase of power of the external rectus muscle by advancement and transplantation of portions of the superior and interior rectus muscles.

Hummelsheim [1] sutured his transplants under Tenon's capsule, but over the insertion of the muscle. He reported 2 cases in which abduction was obtained, but he did not say how much. Gifford [2] reviewed the literature up to 1929 and reported 4 cases of his own. He did a complete

Read at a meeting of the Section on Ophthalmology, College of Physicians of Philadelphia, April 15, 1943.

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tenotomy of the internal rectus muscle, with transplantation of the outer thirds of the superior and inferior rectus muscles beneath and behind the normal insertion of the paralyzed external rectus muscle. O'Connor [3] split the tendon of the paralyzed external rectus muscle into three parts, the two outer portions being cut 10 mm. from the insertion and the transplants sutured to these cut ends. The middle third of the muscle was shortened. Peter [4] advanced the whole paralyzed muscle and split the end into halves, the upper half being carried forward and upward and attached to the outer portion of the superior rectus muscle and the lower half being united to the outer half of the inferior rectus muscle. Woodruff [5] reported 2 cases in which he sutured the transplant to the tendon of the paralyzed muscle but obtained no abduction. Todd,[6] Wiener [7] and Tenner [8] each reported a case in which a similar operation was performed and slight abduction obtained. Turner [9] reported a case in which the transplanted tendon tongues were sutured together beneath the paralyzed muscle, without any abduction being obtained and within balance of the vertically acting muscles remaining.

Franklin and Cordes [10] reported 2 cases in which they sutured the two transplanted tendons beneath the surface of the paralyzed muscle; in 1 case 27 degrees, and in the other 15 degrees, of abduction was obtained. This seems to be the first definite statement as to the degree of external rotation resulting from any of these procedures. Elschnig [11] reported 4 cases in which the Hummelsheim technic had been followed, with no effect on outward rotation. Key [12] reported a case of paralysis of the sixth nerve in which 15 degrees of outward rotation was obtained by transplantation of the tendon.

In 1936 Wiener [13] described a new procedure for this operation, in which the external rectus muscle was cut off 15 mm. from its insertion and the portion left attached to the globe split in half, the upper half being sutured to the tendon of the intact superior rectus muscle and the lower half to the tendon of the intact inferior rectus muscle. He claimed good results, but no measurements were given. Smith [14] used Hummelsheim's original technic in 4 cases and reported that he obtained as much as 30 degrees of abduction. Eber [15] reported 2 cases in which this method was employed and abductions of 30 and 40 degrees were obtained.

From 1929 to 1940, Gifford [16] operated in 16 cases, his technic being essentially the same as that he reported in 1929, except that he used half of the vertically acting muscles for his transplants. The greatest amount of abduction he obtained in any of these cases was 35 to 40 degrees, the condition in 1 case being due to acquired syphilis. In cases of traumatic origin the abduction varied from zero to 22 degrees. In some of these cases the internal rectus muscle was tenotomized, and in others recession was carried out.

Recently, Payne [17] reported a case of convergence of the left eye with diplopia, which was not of traumatic origin and the cause of which was never discovered. The outer halves of the superior and inferior rectus muscles were sutured to the split ends of the external rectus muscle, which was advanced also to a new position, and later a 2 mm. recession of the internal rectus muscle was done. The result was 43 degrees of abduction on the perimeter and esotropia of 4 degrees, with hypertropia of 6 degrees in the left eye. The last defect was overcome by prisms.

Payne also reported a second case of palsy of the external rectus muscle due to syphilis. In this case only recession of the internal rectus and resection of the external rectus muscles were done, and a good result was obtained, with no diplopia in any direction.

1530 Locust Street.

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Obituaries

GEORGE LINDSAY JOHNSON, M.D.

1853-1943

George Lindsay Johnson, M.A., M.D., B.C. (Cantab.), F.R.C.S., Honorary Fellow of the Friedrich Wilhelm Academy of Scientific Research, Berlin, and Honorary Fellow of the Royal Society of Italy, died in Durban, Natal, South Africa, in July 1943, where he had been living and practicing since leaving London, shortly after 1900. He was born near Manchester, England, July 10, 1853, and was educated at Amersham Hall, near Reading, England; the University of Bonn; Kornthal in Württemberg, Germany; Owens College, Manchester, England, and Caius College, Cambridge.

Dr. Johnson made a special study of optics and did a vast amount of research in that science. He undertook a great deal of work for the Elder Brethren of Trinity House in connection with the illumination of lighthouses and the best kind of glasses for protection of the eyes of lighthouse keepers when adjusting their powerful lamps. During the first world war he devised a number of optical instruments for the British government and wrote a book on range finding for the Japanese government. He served as surgeon during two and a half years in World War I. His earlier work, and that for which he is best known in the photographic world, was in connection with the construction of lenses and color photography.

In ophthalmic circles Dr. Johnson is best known for monographs on mammalian eyes and on those of reptiles and amphibia. For these contributions he received the honorary fellowships of the Berlin and Italian societies. He was also elected a honorary fellow of the American Academy of Ophthalmology and Otolaryngology. He was elected a fellow of the Royal Photographic Society and obtained the gold medal at the St. Louis exhibition, as well as the bronze medal. He was for ten years an examiner in theoretic and applied optics to the S. M. C., of London, and ophthalmic surgeon to the Western General Hospital Dispensary, which appointment he held for twenty years. He was also ophthalmic surgeon to the West End Hospital for Nervous Diseases and to various charities. He was a frequent contributor to the old ARCHIVES. Among his many works are: "Treatise on Glaucoma," "Photographic Optics and Colour photography," "Photography in natural Colours" (four editions), "Pocket Atlas and Textbook on the Fundus Oculi" (two editions). "Observations on European Leprosy," "Ophthalmology of the Mammalia" (1901), "Ophthalmology of Reptilia and Amphibia" (1942) and "Trachoma." He was also the inventor of various ophthalmic instruments.

He made a thorough scientific investigation of what are known as occult phenomena connected with the subconscious mind of man and gathered and sifted all available information relating to survival after death and the communication between the departed in the etheric world and persons on earth. He embodied his researches in a large volume, illustrated by photographs (The Great Problem, London, Rider, Rider & Co., 1935; New York, Harper Brothers, 1936).

This remarkable career was possible only to a man with a mind gifted beyond the ordinary, with a keen imagination, interest and great endurance and driving power. He made the thirteenth chapter of St. Paul's "First Epistle to the Corinthians" his rule of conduct and avoided worry. His guiding rule was: "Do all the good you can, and make no fuss about it. What you believe is of no consequence; what you do is the only thing that matters."

ARNOLD KNAPP.

RAYNER DERRY BATTEN, M.D.

1858-1943

Dr. Rayner Derry Batten, who died on Oct. 22, 1943, was born in Plymouth, England. He took his medical degree in 1886 and was in general practice for a number of years, although at the same time he did ophthalmic work at Moorfields and in the end gave up his general practice for ophthalmologic work. He was a surgeon at the Western Ophthalmic Hospital, in London, for thirty-three years. He became vice president of the Ophthalmological Society of the United Kingdom and a member of the council of the Oxford Ophthalmological Congress. He was essentially a clinician; though his operative skill was considerable, he suggested that the technic of ophthalmic surgery should be confined to the few, in other words, that the practice of ophthalmology should be shared between the ophthalmic physician and the ophthalmic surgeon.

He is well known for a fixation fork and a hydrophthalmoscope, which was originally devised to examine the fundus in cases of high myopia. He was instrumental, with the aid of his brother, who was an artist, in training fundus artists, and the first class was trained under his supervision. From this group developed the school for such training. He was perhaps best known in connection with investigations which he undertook with his brother, F. E. Batten, the neurologist, on heredomacular degeneration.

ARNOLD KNAPP.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Biochemistry

THE ROLE OF IRON, COPPER, ZINC, AND MANGANESE IN THE METABOLISM OF THE OCULAR TISSUES, WITH SPECIAL REFERENCE TO THE LENS. F. WARREN TAUBER and A. C. KRAUSE, Am. J. Ophth. 26: 260 (March) 1943.

From their experiments on the eyes of cattle, Tauber and Krause give the following summary: "The results of quantitative determinations of iron, copper, manganese, and zinc in the ocular tissues are recorded. The physiologic activity of these elements in relation to their mechanism in various biologic systems and of their effect on ocular metabolism with special reference to lens is briefly discussed." W. S. REESE.

Conjunctiva

CHEMOTHERAPY IN ACUTE GONOCOCCAL CONJUNCTIVITIS. L. K. SWEET, Am. J. Ophth. 25: 1487 (Dec.) 1942.

Sweet reports his observations and the results of treatment of 102 patients suffering from acute gonococcic conjunctivitis. He concludes that the use of sulfanilamide should be discontinued and that sulfathiazole may be toxic to the conjunctiva; he also claims there is little choice between sulfapyridine and sulfadiazine except that the latter is reported to be less toxic. W. S. REESE.

PARINAUD'S OCULOGLANDULAR SYNDROME. M. A. WOOD, Am. J. Ophth. 26: 141 (Feb.) 1943.

Wood reports 2 cases of Parinaud's conjunctivitis, although several laboratory tests failed to establish a diagnosis of the disease. In 1 case a positive reaction for tularemia was obtained in an agglutination test, but subsequent tests gave negative results. W. S. REESE.

STUDIES ON THE INFECTIVITY OF TRACHOMA: FURTHER EXPERIMENTS ON THE ANTIGENICITY OF THE VIRUS. L. A. JULIANELLE, Am. J. Ophth. 26: 378 (April) 1943.

Julianelle gives the following summary of further experiments on the antigenicity of the virus.

"The present report records the attempts made to adsorb trachomatous virus on bacterial cells in order to render it agglutinable by 'antisera' obtained from patients, experimentally infected monkeys and artificially immunized monkeys and rabbits. Other attempts to demonstrate serologic reactivity by fixation of combined antigen-antibody on collodion particles were likewise unsuccessful. The observations suggest that such sera are devoid of antiviral antibodies, thus confirming the results of a previous study." W. ZENTMAYER.

Cornea and Sclera

VIRUS ISOLATED FROM PEMPHIGUSLIKE KERATOCONJUNCTIVITIS. E. GALLARDO and L. H. HARDY, Am. J. Ophth. 26: 343 (April) 1943.

The authors give the following summary of their clinical and experimental study in a case of pemphigus-like keratoconjunctivitis:

"1. A case of severe chronic cicatrizing keratoconjunctivitis with pannus, similar in clinical appearance and course to ocular pemphigus, is described. A presumptive diagnosis of ocular pemphigus was made on the basis of (*a*) the slow progressive cicatrization most marked in the lower fornices, (*b*) the periods of remission, and (*c*) the absence of follicles, inclusion bodies, or typical pannus of trachoma. The skin and other mucous membranes were not involved.

"2. A virus, designated as S virus, close to it not identical with vaccinia virus, was isolated from conjunctival scrapings during three different periods of exacerbation of the disease. Typical elementary bodies and cytoplasmic inclusions like those of vaccinia were found.

"3. The possibility of a laboratory contamination with rabbit pox or vaccinia was considered but could be ruled out.

"4. The virus was isolated both by rabbit-cornea and mouse-brain inoculations as well as by inoculation of the chorioallantois of the developing chick embryo. The close relationship to vaccinia virus was shown by neutralization tests in which vaccinia-immune serum neutralized the S virus and anti-S serum neutralized vaccinia virus.

"5. The relationship of the virus to the keratoconjunctivitis must remain an open question until observations on other similar cases become available." W. ZENTMAYER.

CORNEAL VASCULARIZATION PROBLEMS. DERRICK VAIL and K. W. ASCHER, Am. J. Ophth. 26: 1025 (Oct.) 1943.

This report is concerned with an extensive study of the corneas of 711 patients seen in the Nutrition Clinic in Birmingham, Ala., and in the outpatient clinic of the department of ophthalmology of the University of Cincinnati Col-

lege of Medicine. Concentric collaterals are engorged parts of the preexistent limbal meshwork. They collect blood from all limbal loops of one entire sector of the limbus, or a part of them, and return this blood from the limbus to the larger conjunctival veins.

Concentric collaterals occurred in 13.3 per cent of patients with manifest, subclinical or suspected vitamin deficiency who were observed in the nutrition clinic. Of 69 persons observed in the ophthalmic clinic of the University of Cincinnati, almost one-half had concentric collaterals. The occurrence of engorged limbal loops and concentric collaterals in each group was more frequent in females and was distributed over all age periods. From these observations no relation can be deduced between any particular type of vitamin deficiency and the presence of concentric collaterals. Of 69 patients selected at random from the Cincinnati group, 37 presented congestion in the limbal region, 31 of whom, predominantly females, showed typical concentric collaterals. The percentage of eyes with concentric collaterals was higher in white persons than in Negroes. There was no relation between the dietary habits and the frequency of vascular congestion in the limbal region. The number of patients showing such congestion was higher among persons receiving a good diet than among those with a poor diet. Even the number of persons with both eyes affected was higher among the well nourished patients.

Although in the Birmingham group, consisting of persons with manifest, subclinical or suspected vitamin deficiency, about one eighth of all patients observed showed concentric collaterals, in the Cincinnati group more than one third of all patients exhibited this sign.

W. Zentmayer.

Groenouw's Corneal Dystrophy. J. O. Wetzel, Am. J. Ophth. **26:** 1183 (Nov.) 1943.

Wetzel gives the following summary:

"Hereditary eye defects have furnished genetic data for many scientific investigations, thereby encouraging the study of such visual impairment. Familial nodular degeneration of the cornea is one of the most interesting of these conditions, though it has not received as much attention as have others which occur more commonly.

"Three types of this condition have been postulated: the circumscribed parenchymal disc dystrophy of Fleischer, the 'lattice' type of Haab and Dimmer, and the nodular dystrophy of Groenouw.

"The introduction of the biomicroscope and slitlamp enabled ophthalmologists to study these lesions *in situ*. The salient characteristic of Groenouw's disease is the presence of minute opacities in the center of the cornea, somewhat elevated above the level of the superficial layer of this structure. These opacities gradually become more dense, so that if the subject lives long enough he becomes entirely blind. The cause is not known.

"The familial incidence of this affection was first noted at the beginning of the present century by Fuchs, and extensively studied by Freund, who followed it through four generations in two family lines.

"No effective treatment has even been discovered, although various, suggested measures have improved the condition of individual patients.

"A case report is offered and a genealogic chart provided showing the incidence of the condition in three generations of the same family."

W. S. Reese.

Experimental Pathology

Changes in Mineral Composition of Rat Lenses with Galactose Cataract. P. W. Salit, K. C. Swan and W. D. Paul, Am. J. Ophth. **25:** 1482 (Dec.) 1942.

Salit, Swan and Paul report their observations on 461 rat lenses, of which 119 were normal, 186 had incomplete cataracts and 156 complete cataracts. The cataracts were induced by feeding the rats relatively large amounts of galactose. In general the changes were similar to those which occur in human senile cataracts.

W. S. Reese.

General

The Vitamins in Ophthalmology. A. J. Baer, Am. J. Ophth. **26:** 286 (March) 1943.

Baer briefly reviews the relation of vitamins A, B. C, D and K to ocular disorders. He concludes that the subject is still controversial and that it must be investigated much further before the action of these substances can be properly evaluated.

W. S. Reese.

Intravenous Pentothal Sodium Anesthesia in Ophthalmology. L. T. Post and E. N. Robertson, Am. J. Ophth. **26:** 1155 (Nov.) 1943.

Post and Robertson feel that pentothal sodium is a satisfactory anesthetic. They give the following summary:

"A brief review of the literature on pentothal sodium anesthesia is presented along with statistical data on 106 operations performed on eye patients in Barnes Hospital under this type of anesthesia. Following this is a discussion of the data."

W. S. Reese.

General Diseases

Focal Infection. A. C. Woods, Am. J. Ophth. **25:** 1423 (Dec.) 1942.

Woods gives the history and vicissitudes of the theory of focal infection and, after reviewing several reports concludes that it is wise to continue to search for foci of infection and to treat

them intelligently, and not to regard their eradication as a cure-all for endogenous ocular disease.

W. S. REESE.

AMAUROSIS FOLLOWING NASAL HEMORRHAGE. A. E. LONG, Am. J. Ophth. 26: 1179 (Nov.) 1943.

Long reports a case of pronounced unilateral visual loss six days after profuse, recurrent nasal hemorrhage. Treatment consisted of administration of miotic drugs and transfusions, with negligible immediate results but with eventual restoration of vision to 2 — /40. The author discusses the pathogenesis of the condition.

W. S. REESE.

ARACHNODACTYLY COMPLICATED BY DISLOCATED LENS AND DEATH FROM RUPTURE OF DISSECTING ANEURYSM OF AORTA. L. E. ETTER and L. P. GLOVER, J. A. M. A. 123: 88 (Sept. 11) 1943.

A man aged 21 presented most of the physiognomic characteristics of the syndrome, namely, bossing of the frontal eminences, prominent supraorbital ridges, protrusion of the upper half of the ears, large chin, high-arched palate, long slender teeth, very long hands and feet, a small amount of subcutaneous fat and a pronounced degree of muscular hypotonia with relaxation of ligaments. The right eye was myopic, with a corrected vision of 20/30, and the lens and fundus were normal. Vision in the left eye was limited to counting fingers at 5 feet (152 cm.) and was corrected to 20/200. The lens was subluxated downward and tilted slightly backward at 12 o'clock. The lens presented peripheral congenital opacities. There were aortic regurgitation with pronounced enlargement of the heart, massive hemopericardium and chronic dissecting aneurysm of the ascending aorta, with acute, fatal rupture into the pericardial sac. The article is illustrated.

W. ZENTMAYER.

Injuries

PROCEDURES AND APPLIANCES THAT ARE HELPFUL IN TREATING INDUSTRIAL OCULAR INJURIES. W. B. CLARK, Am. J. Ophth. 26: 1054 (Oct.) 1943.

Clark has found the Mueller shield, now made of plastic, of advantage in the treatment of burns of the eye. It separates the bulbar and the palpebral conjunctiva and prevents the formation of symblepharon; it protects the damaged cornea from the conjunctival surface of the lids, which is also usually damaged in cases of chemical burn. It not only prevents but has corrected cicatricial ectropion that followed a burn of the lids. The author's method of using the shield is described.

A suture for closing corneal and scleral lacerations is described. Corresponding sutures are placed parallel with the wound on each side, and the two ends are tied across the wound.

W. ZENTMAYER.

MEASURING EYE FLASH FROM ARC WELDING. V. E. KINSEY, D. G. COGAN and P. DRINKER, J. A. M. A. 123: 403 (Oct. 16) 1943.

The authors' purpose in the present study was to derive a practical rule whereby one can estimate in terms of time, intensity of radiation and distance the safety of any exposure to a welding arc.

In order to make the data readily applicable to operating conditions, an ordinary Weston photographic light meter was calibrated in foot candles and used as a measure of dosage. The intensity of the radiations varied threefold or fourfold from moment to moment, so that it was necessary to estimate the average intensity throughout the period of exposure. The average meter reading, expressed in foot candles, multiplied by the duration of exposure, given in minutes, is used as an "exposure" coefficient, or time-intensity factor. The units thus become foot candle–minutes.

A light meter calibrated in foot candles was found to give an adequate, although arbitrary, measure of the doses of radiation from electric welding arcs which produce ocular injury. The exposures to such arcs necessary to produce minimal ocular signs and symptoms in rabbits, dogs and human beings have been measured. As to time of exposure and intensity of radiation, a minimum standard of safety for men in the neighborhood of electric welding arcs has been recommended as one-tenth that required to produce minimal ocular effects.

W. ZENTMAYER.

INTRAOCULAR FOREIGN BODIES IN PEACETIME AND IN WARTIME AND THE PROBLEM OF THEIR REMOVAL. A. I. POKROWSKY, Vestnik Oftal. 22: 5, 1943.

One hundred and twenty-five cases of perforating injuries to the eye in wartime and as many cases of industrial injuries to the eyes in peacetime served as the material for this paper. In all cases the presence of the foreign body in the eye was confirmed by roentgenographic examination.

The intraocular foreign bodies of prewar times were magnetic in about 85 per cent of cases, while those of wartime were magnetic in only about 45 per cent of cases. The second characteristic feature of intraocular foreign bodies of wartime was their size. Small, light weight foreign bodies were predominant, and the ratio to the large foreign bodies of civilian life was about 2:1. Third, the intraocular foreign bodies of wartime were frequently multiple. Double perforations of the eyeball were also more frequent in war injuries than in industrial trauma. The foreign body was usually removed within the first week after injury in cases of industrial accidents, while in cases of war injuries the body was not removed for three to ten weeks because of the frequent delay in military hospitals and the transportation problems.

Pokrowsky stresses the importance of early removal of intraocular foreign bodies in order to prevent their encapsulation and to avert inflammation of the eyeball. Removal of intraocular foreign bodies in peacetime was performed with the electromagnet by the anterior route in about 82 per cent of cases, while in wartime good results were obtained by this method in 64 per cent of cases. The method of choice for the removal of intraocular foreign bodies during the war was the diascleral posterior route. The Comberg-Baltin prosthesis for localization of the foreign body was used and is considered to be most adequate. Operation by the posterior route frequently prevented exacerbation of the inflammatory process and entanglement of the foreign body in the ciliary processes, and recovery was more rapid than with operation by the anterior route.

Pokrowsky usually applied prophylactic diathermocoagulation before the scleral incision for prevention of consequent retinal detachment and intraocular hemorrhages. Careful and detailed localization is important because the majority of the intraocular foreign bodies are nonmagnetic.

O. SITCHEVSKA.

Neurology

CHRONIC OPHTHALMOPLEGIA EXTERNA. I. FAGIN, Am. J. Ophth. 25: 968 (Aug.) 1942.

Fagin classifies the causes of chronic external ophthalmoplegia and reports a case of chronic progressive ophthalmoplegia externa, due presumably to nuclear sclerosis.

W. S. REESE.

Retina and Optic Nerve

ANGIOMATOSIS RETINAE (VON HIPPEL–LINDAU DISEASE): REPORT ON A GENEALOGIC TREE. W. RUMBAUR, Klin. Monatsbl. f. Augenh. 106: 168 (Feb.) 1941.

Five members of a family presented symptoms of angiomatosis of the retina, and 6 of 15 other members of the same family had anomalies of other parts of the body, such as tumor of the pancreas, complicated by angiomatosis retinae in 1 case and by diabetes in another, and 1 had a tumor of the brain. Three other members had lesions of an allied nature: One had juvenile presclerosis with retinal angiomatosis; 1 coloboma of the iris, microphthalmos and defective speech, and another, microcephalus and idiocy. Members of four generations were examined.

The first 5 patients mentioned presented angiomatosis of the retina in different stages, varying from the prodromal phase without angiomatous nodules in 1 patient to partial degeneration of the retina with rapid decrease of function in another. The last-named patient was the second to present the nodule behind the retina.

In the fifth patient recovery occurred in one eye, but in the other the process terminated in detachment of the retina. The case is proof of the synchronous occurrence in the same patient of the benign form of the disease in one eye and of the malignant form in the other. The condition, furthermore, was complicated by an adenoma of the pancreas; the tumor had remained without recurrence for fifteen years, after having been reduced in size by removal of a specimen for biopsy.

Observation of the patients led Rumbaur to express the belief that the vascular changes are primary and that the angiomatous nodules form secondarily at the junction, or anastomosis, of arteries and diseased veins. So-called isolated angiomatous nodules arise from fine capillaries, which cannot be observed with the ophthalmoscope; they may be enlarged capillaroglomeruli, as described by Czermak, von Hippel and other investigators.

In the fourth patient the retinal angiomatosis healed spontaneously. The fifth patient may have had a similar recovery in the one eye, for "empty," pale nodules were observed. Their presence permits the conclusion that the prognosis of retinal angiomatosis is not always unfavorable. The von Hippel–Lindau syndrome is due to specific hereditary factors.

The author undertook treatment of some of his patients, a satisfactory result being obtained with diathermy, in some instances. In 1 patient he attacked the nodule directly with the diathermy needle, destroying it with coagulation. He produced healing of numerous secondary changes in the retina by coagulation of a large angiomatous nodule. In this manner the tumor could be reduced in size by operation and smaller nodules be made to disappear.

K. L. STOLL.

Society Transactions

Edited By Dr. W. L. Benedict

CANADIAN OPHTHALMOLOGIC SOCIETY

Colin A. Campbell, M.D., *President*

Sixth Annual Meeting, Sept. 25, 1943

Color Photographs of External Lesions of the Eye. Dr. A. Lloyd Morgan, Toronto.

Corneoscleral Sutures. Dr. R. J. P. McCulloch, Toronto.

The use of sutures to close the corneal incision in operations for cataract is steadily increasing. The chief argument against their use is the trauma inflicted by their insertion, which adds a danger to the operation greater than the benefits obtained from their use. The sutures can be inserted in the cornea without great difficulty or danger. It is the passage of the needle through the scleral tissue that involves danger of rupture of the zonule or disturbance of the vitreous. In this paper is described a method by which this danger may be avoided. Two or more silk loops are inserted in the scleral tissue before the section is made; these loops are used later to draw the sclerocorneal sutures into position.

The technic was illustrated by diagrams and colored moving pictures of two operations.

Sulfonamide Compounds in Treatment of Local Ocular Conditions. Dr. Alson E. Braley, New York.

The results obtained in 568 cases of acute and chronic conjunctivitis treated with sulfathiazole, sulfadiazine, sulfapyrazine, sulfamethazine and penicillin in the form of ointments are reported.

The sulfonamide compounds were used in 5 per cent concentration in 25 per cent anhydrous wool fat and 75 per cent petrolatum. Penicillin salts of sodium, barium and calcium were employed in a concentration equivalent to 250 or 500 Florey units per gram in a water-soluble base. Treatment was administered every four hours.

Some cases of individual sensitivity occurred with sulfathiazole, but the disturbance cleared up when one of the other drugs was substituted. The majority of the patients were from the Vanderbilt Clinic and Letchworth Village, Thiells, N. Y.

Acute Conjunctivitis (126 cases).—The organisms most commonly encountered were Staphylococcus aureus, the pneumococcus and the influenza bacillus.

Nearly all the preparations of the sulfonamide compounds gave good results. The acute staphylococcic conjunctivitis was the most resistant. Results, however, in cases of this infection were better with sulfonamide therapy than with the usual treatment (1 per cent silver nitrate and a 1 : 5,000 concentration of mercuric oxycyanide). There was a tendency for the condition to become chronic with use of the agents last mentioned.

Chronic Catarrhal Conjunctivitis.—Chronic conjunctivitis, always a therapeutic problem, was best controlled by local use of sulfathiazole, provided treatment was continuous. Relapses occurred with its discontinuance. Sometimes a change to a different sulfonamide compound had a pronounced effect. When cultures of staphylococcus were obtained during the use of sulfathiazole, penicillin was remarkably effective; it is perhaps the drug of choice. There were 4 cases of therapeutic failure. Sulfathiazole was more effective than penicillin against the diplobacilli. In treatment of streptococcic chronic membranous conjunctivitis results with any of the drugs were disappointing. In the cases of pneumococcic infection both sulfathiazole and penicillin were effective.

Chronic Blepharitis.—In 24 cases sulfathiazole was used, in 9 of which there was recurrence. Treatment with one of the other drugs was then employed in these cases. The staphylococcus and diplobacillus were the organisms most commonly seen. Sodium sulfadiazine appeared to give better results than sulfathiazole. Penicillin was the most effective against the staphylococcus.

DISCUSSION

Dr. W. W. Wright, Toronto: Can Dr. Braley state whether local application of the sulfonamide compounds in the eye is likely to set up any sensitivity, so that internal administration for a serious condition, such as pneumonia, would be contraindicated? Some internists have stated that ophthalmologists should not use the sulfonamide drugs as freely as they do.

Dr. Alson E. Braley, New York: I have only 1 case to illustrate that point. A woman was sensitized to sulfathiazole. She had been given local treatment with sulfathiazole, as a result of which severe sensitivity to the drug developed; oral administration of sulfathiazole was followed

by an infection of the palate. She had had a severe reaction, it is true. Whether or not she was sensitized by local use of the compound I am not sure. She was also sensitive to sulfadiazine, which was given orally. I then used sulfacetimide, and she responded well. Certainly, with the choice of sulfonamide compounds available, I see no reason that they cannot be used locally. There are plenty of other sulfonamide drugs for treatment of pneumonia. There is no direct carry-over from sulfathiazole to sulfacetimide, for the two substances have a different principle.

Primary Tumors of the Lacrimal Gland. DR. J. A. MACMILLAN, Montreal.

Three cases are reported. Two of these were instances of adenocarcinoma of the cylindroma type, in both of which females were affected. One of these patients was 30 and the other 64 years of age. In each case the tumor was removed—in the first three years, and in the second four months, after the appearance of the first sign, proptosis. In the second case there was local recurrence, with extensive removal of the overlying bone, one year after the original removal of the growth. In both cases roentgen and radium therapy was employed, and death occurred from intracranial extension eight years after the first appearance of the proptosis. The third case was one of mixed cell tumor in a man aged 29. The gland was removed four months after the first sign, proptosis. Seven months later there was a recurrence in the orbit, and a second operation was performed, with incomplete removal. Permission for exenteration of the orbital contents was refused. The patient is at present receiving roentgen therapy. The term "mixed tumor" should be reserved for the growths with mixed cell types and should not be applied to those which show only columns of epithelial cells with a tendency to form glands. Such a tumor should be called cylindroma, or adenocarcinoma of the cylindroma type. In cases of proptosis in which the presence of a tumor is suspected or cannot be excluded, the orbit should be explored early, when complete removal may be accomplished.

Microscopic slides of the tumors and cell types in the 3 cases were presented.

Ophthalmologic Research in the Royal Canadian Navy. SURGEON CAPTAIN C. H. BEST and SURGEON COMMANDER D. Y. SOLANDT.

The first problem involving vision of officers and ratings in the Royal Canadian Navy to be attacked by the research group was concerned with the lighting at night of instruments, charts and the like. Studies revealed that a certain wave-length at the red end of the spectrum was the most desirable, and, after trials at sea, it was formally adopted for lighting by the Royal Canadian Navy. The Royal Navy and the United States Navy subsequently utilized a similar system of lighting.

A new color vision lantern for the naval service has been devised and officially adopted. A modification of the Hecht adaptometer for tests of night vision is now in service. Glassless eye shields for protection against winds of high velocity have been devised and accepted by the naval services. The fitting of glasses and other problems have been studied by ophthalmologists and opticians attached to the research group.

These various activities were briefly reported.

Orthoptics in Aviation. SQUADRON LEADER JOHN V. V. NICHOLLS, R.C.A.F.

Orthoptic training has considerable value for a small, but fairly definite, group of carefully selected patients. Its value is limited to those who have an imbalance of the ocular muscles sufficient to disturb their stability of fusion and the dependability of their stereopsis, and who have not compensated for this deficiency by the development of accurate monocular depth perception.

Technic of Enucleation of the Eye, with Implantation of a Prothesis. DR. W. W. WRIGHT, Toronto.

The following points in the technic of the operation of enucleation were stressed: (1) use of local anesthesia whenever possible; (2) undermining and preservation of as much of the conjunctiva as possible and the placing of an identifying black silk suture above and below the margin of the conjunctiva; (3) use of a snare instead of scissors for severance of the optic nerve and vessels, the instrument being best introduced at the nasal side of the eye; (4) deep placement of oblique mattress catgut sutures, instead of the more common purse string suture, around and 8 mm. behind the edge of Tenon's capsule; (5) use of a suitable prothesis, preferably a solid, pure glass ball 16 to 18 mm. in diameter, and (6) importance of a pressure bandage, made of fluffed-up gauze, completely covered by adhesive plaster and left in place for four or five days.

Relation of Ariboflavinosis and Circumcorneal Vascularization as Observed in the Navy. SURGEON COMMANDER E. A. AMOS, R.C.N.V.R.

A short review and an analysis of the literature were presented. The difference between the nutritional and the ophthalmic viewpoint was stressed. The work done on this subject in the Royal Canadian Navy was reviewed.

I believe that circumcorneal vascularization alone is not pathognomonic of vitamin deficiency, and may be due to several causes, but that circumcorneal vascularization in conjunction with photophobia, lacrimation and some impairment of visual acuity and in the absence of

errors of refraction or muscular imbalances is an ocular syndrome which responds readily to riboflavin therapy. This opinion is based on the results for 3,725 men of binocular microscopic examination with slit lamp illumination. A subjective history was always taken, and 383 of the men were given riboflavin orally.

DISCUSSION

SQUADRON LEADER JOHN V. V. NICHOLLS, R.C.A.F.: I was much attracted by the presentation of this problem by Surgeon Commander Amos. He has been conservative in his treatment, and I think wisely, in view of the discrepancy of opinion concerning the causal relation of ariboflavinosis and corneal vascularization. Group Captain Tisdale and I have a series of 52 patients, whom we divided into two groups. One, an experimental group of 32 men, was given 10 mg. of riboflavin daily. The other, the control group, of 19 men, did not receive any riboflavin. They were examined at the beginning of the experiment and, again, two months later. In the experimental group, the condition of 45.4 per cent of the men was unchanged at the end of two months' administration of riboflavin; that of 24.2 per cent was worse and that of 27.3 per cent was better. With respect to the control group, who were at sea, the state of 36.8 per cent was unchanged, as compared with 45.4 per cent of the experimental group; the condition of 46 per cent was worse, as compared with 24 per cent of the experimental group, and that of 26 per cent was better, as compared with 27 per cent of the experimental group. This series is small, but the figures show that in this particular group the administration of riboflavin had no effect on the corneal vascularization.

Importance of Adequate Clinical Records for Genetic Analysis of Hereditary Diseases of the Eye. DR. MADGE THURLOW MACKLIN, London, Ontario.

The importance of heredity in diseases of the eye was briefly reviewed. The part played by the ophthalmologist in obtaining adequate histories for analysis by trained geneticists was discussed, and the type of family history which is desirable was outlined. The following points should be noted in history taking: relationship of the parents of the patient; presence or absence of the disease in other members of the family; number of brothers and sisters of the patient; ages of the siblings and whether they are affected; age of onset of the disease in the various members of the family; variations in the manifestations of the disease in different members of the family, and any other related disease processes occurring in the family.

Clinical records illustrated the value of adequate histories and the uselessness of incomplete records.

Retinal Arterial Tension Associated with Epilepsy. DR. G. A. STUART RAMSEY and DR. HADDOW M. KEITH, Montreal.

Some observers have asserted that epileptic patients show, even between attacks, more variability in pressure in the retinal arteries than in the systemic arteries. They also contended that removal of the carotid body tends to stabilize this pressure, and at a higher level. In some cases this stabilization brings about cure or improvement.

In an evaluation of these statements, 96 epileptic patients and 43 control subjects were studied. Tonoscopic examinations were made, both by the instrumental method and by the technic of Baillart.

The results agreed in the main with those of other observers, but some differences were noted. There was a greater average variability in pressure in the retinal arteries in epileptic than in control subjects, but individual control subjects showed as great variability as any of the epileptic patients.

After removal of the carotid body in the epileptic patients the variability did not decrease permanently, and though the tension in the retinal arteries tended to remain higher for some time after the operation, it returned to its preoperative level in about six months.

Amaurosis Caused by Blastocytoma of the Adrenal Gland. DR. COLIN A. CAMPBELL, Toronto.

Blastocytoma, or neurocytoma, of the adrenal, once classified as sarcoma, occurs in young children, is highly malignant and is of interest to ophthalmology in that the first diagnostic signs are usually in and about the eyes. Metastases early attack the cranial bones and the orbit, causing hemorrhagic discoloration of the eyelids, ptosis, proptosis, loss of vision and swellings on the bones of the skull. Fever, "rheumatic" pains and anemia are usual.

In the case presented, the first cranial symptom was loss of vision, progressing to amaurosis in about ten days, before the appearance of local orbital or fundic changes of any kind.

Colored Moving Pictures of Plastic Surgical Procedures on the Eye. MAJOR J. P. GILHOOLY, R.C.A.M.C., Ottawa, Ontario.

Moving pictures of operations for correction of strabismus and ptosis and blepharoplasty were shown. It was emphasized that plastic surgery of the eye should remain in the field of ophthalmology and should be the responsibility of the ophthalmic surgeon.

The literature was reviewed; 3 additional cases, from the Hospital for Sick Children, Toronto, were recorded, and an autopsy report, by permission of Dr. I. H. Erb, was given.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

FRANK C. KEIL, M.D., *Chairman*

WILLIS S. KNIGHTON, M.D., *Secretary*

Jan. 17, 1944

Recurrence of Fibrosarcoma of the Orbit Seven Years After Removal: Results of Roentgen Irradiation. DR. ABRAHAM L. KORNZWEIG (by invitation).

A woman aged 35 was first seen in February 1935 with exophthalmos and ptosis of the left eye with pain. The condition had become progressively worse during the preceding two years. A large encapsulated growth was observed to be attached to the orbital wall in the region of the sphenoid fissure and was removed. The pathologic diagnosis was fibrosarcoma of low grade malignancy.

The patient did well until August 1942, when she noticed gradual ptosis of the left eye, with diminishing vision and diplopia on upward gaze. In February 1943 a tentative diagnosis of recurrence of the fibrosarcoma was made, and exenteration of the orbital contents was advised. When the patient refused, twenty-nine roentgen ray treatments were given over a period of fifty days, with a total dose of 5,400 r in air, equally divided above, below and to the right and left sides of the orbit.

Exophthalmos, the amount of which measured 21 mm. in the left eye, as compared with 18 mm. in the right eye, gradually diminished. On May 12 the amount measured 18 mm. in each eye. On September 13 enophthalmos developed, the amount measuring 16 mm. in the left eye and 18 mm. in the right eye. Ocular motility, which was limited in all directions before treatment, had improved almost to normal. Vision in the left eye, which was 20/50 at first, diminished to 20/200 and then improved to 20/70. There were dermatitis around the left eye and swelling and redness of the conjunctiva. All the cilia and the hair of the eyebrow fell out. The retina was mottled in the macular region, and the optic disk was pale. Today, eight months after treatment, the tumor seems to have disappeared.

DISCUSSION

DR. JOSEPH LAVAL: The case which Dr. Kornzweig presented reminds me of a similar case of a young woman whom I first saw nine and a half years ago, when she was 12 years old. A small mass, about the size of a large pea was present at the upper inner angle of the left orbit. The skin over it was freely movable. Roentgenographic examination and clinical and laboratory tests revealed nothing abnormal. The mass was removed, with the use of local anesthesia, but I was sure that some of the tumor was left behind, deep in the orbit. Microscopic examination showed that the growth was cellular, with many mitotic figures. It was not fibrous as was the tumor Dr. Kornzweig described. The diagnosis was myxosarcoma.

The girl received roentgen therapy at Memorial Hospital. Thirteen treatments, of 300 r each were given over a period of four weeks. The result was good. There has been no recurrence in nine and a half years. She has loss of the eyebrows and lashes, a cataract and diminution in tearing, but the cosmetic result is much better than that of exenteration. It is important to remember that sarcoma is amenable to treatment with roentgen rays; the tumor does not have to be a lymphosarcoma.

Anomalies of Fusion Associated with Aniseikonia: A Preliminary Report. MISS EDNA KNAUBER (by invitation).

Thirty-five patients with anomalies of fusion were selected for special study when ordinary fusion training methods failed to relieve their symptoms or to improve their ability to coordinate. Eighty-five per cent of these patients had exophoria or exotropia. Headache, photophobia and discomfort in reading were the most frequent symptoms; diplopia, car sickness and dislike ot moving objects were less common. There was no constant relation between the amount or kind of refractive error and the muscular imbalance. Orthoptic treatment was given for four weeks to four months, with no improvement in the range of fusion. Only 1 patient acquired greater powers of convergence.

Each patient was found to have aniseikonia, the difference in the relative size of the two retinal images varying from 0.75 to 5 per cent and being about equally divided between the vertical and the horizontal meridians. The examinations were made at the New York Eye and Ear Infirmary.

Two cases are reported in which correction of the aniseikonia gave relief from the subjective symptoms, without any change in the basic muscular deviations for 6 meter and for 33 centimeter distances. In 1 case the exotropia of 30 prism diopters for distances beyond 6 meters became an exophoria of 14 prism diopters after the patient wore the correcting eikonic lenses.

Some of the patients wearing these correcting lenses are still receiving fusion training and are improving in functional ability, with fewer subjective symptoms. Others have had such relief that they have not returned for further treatment. This improvement seems to indicate a place for the correction of aniseikonia in the treatment of fusion anomalies which do not respond to ordinary orthoptic measures.

DISCUSSION

DR. HUNTER H. ROMAINE (by invitation): I am unable to report having obtained any "cures"

similar to those Miss Knauber has described during the short time in which I have been treating patients with clinical aniseikonia. The greatest problem presented by patients with muscular imbalance involves the stabilization of fixation. Correction of aniseikonia strengthens fusion, but it is exceedingly difficult to get a satisfactory result in a purely subjective examination, when fixation is difficult and fusion is imperfect as the result of a motor anomaly. Sensitivity to the test is usually poor, and variations in the results are great. The only way by which these factors may be overcome is by repeated examination, with correction of as much aniseikonia as possible at each successive test. Economically this has its disadvantages. Correction of aniseikonia may aid in the treatment of selected patients with motor anomalies, but one should not depend on it to the exclusion of other methods of therapy.

Pupillographic Studies: I. Pupillary Reactions of the Seemingly Unaffected Eye in Clinically Unilateral Simple Glaucoma; Pupillographic Contributions to the Diagnosis of Glaucoma in the Preclinical Stage. Dr. Otto Lowenstein (by invitation) and Dr. Mark J. Schoenberg.

This paper will be published in full, with discussion, in a later issue of the Archives.

Treatment of Glaucoma. Dr. Paul Chandler, Boston (by invitation).

This paper will be published in full, with discussion, in a later issue of the Archives.

Diagnostic Value of Monocular Occlusion. Dr. Kenneth Roper and Dr. Robert E. Bannon, Hanover, N. H. (by invitation).

This paper will be published in full in a later issue of the Archives.

Correspondence

BINOCULAR REFRACTION WITH CROSS CYLINDER TECHNIC

To the Editor:—Major H. Saul Sugar, in his article "Binocular Refraction with Cross Cylinder Technic," published in the January issue (ARCH. OPHTH. **31**: 34, 1944), states that "many persons who wear corrective lenses the prescription for which has been determined by accurate monocular refraction and who do not have abnormal lateral or vertical phorias are uncomfortable during binocular vision." He then asserts that "the trouble is due to changes in the axes of the cylinders when both eyes are used together for distant vision and during convergence accommodation."

On page 37 he further states that the principle of "spherical equivalents" is important in the obtaining of comfortable binocular vision in cases of anisometropia. This statement is followed by a brief résumé of the principle of spherical equivalents and the rule for the reduction of the cylinder.

Refractionists have long known that in cases both of high and of moderately high astigmatism the patient may experience both monocular or binocular confusion when first wearing the correction and that approximately the same visual acuity may be obtained by reduction of the cylindric correction one-half if such confusion occurs. In other words, as stated by J. T. Maxwell (Outline of Ocular Refraction, Omaha, Medical Publishing Co., 1937, page 160): ". . . Add algebraically to the spherical component one half the difference between the full cylindrical correction and the reduced cylinder 'chosen'."

So far so good, but Major Sugar then proceeds to cite 4 cases in which the patient would not accept corrections determined by monocular refraction. He apparently ignores the obvious anisometropic aspects of these corrections at the reading level and states that the patients were all made comfortable by use of the rule of spherical equivalents and reduction of the cylinders. There should be some discussion of the implications of this important statement.

Despite the fact that Major Sugar's introductory sentences state that "in many persons who wear corrective lenses the prescription for which has been determined by accurate monocular refraction and who do not have abnormal lateral or vertical phorias are uncomfortable during binocular vision," in 3 of the 4 cases cited severe vertical heterophoria was manifested and in the remaining case lateral heterophoria prism base out was induced at the reading level.

I shall consider the cases in order:

CASE 1.—Private F. W., aged 23. Correction was as follows:

Right eye: — 2.75 D. sph. ⊃ + 2.00 D. cyl. axis 100.

Left Eye: — 1.50 D. sph. ⊃ + 0.25 D. cyl. axis 90.

This prescription caused severe discomfort binocularly! Why indeed should it not? At the reading level (10 mm. below the optical center and probably 12 mm. below as determined by mirror reflection by the Univis Lens Company) this prescription has an induced vertical heterophoria of 1.25 prism diopters.

What this prescription obviously calls for is not a reduction in the sphere-cylinder combination by the use of the rule of spherical equivalents (as these cylinders are not high) but the addition of a "slabbed-off prism" of 1.25 diopters base up for the right eye, to get rid of the anisometropia at the reading level; either that or the prescription of two pairs of glasses, one of which, the reading pair, has dropped optical centers.

Too often it is wrongly asserted that a patient can tolerate a vertical imbalance of 1 degree of prism at the reading level. This is untrue, since fusional amplitude is often nonexistent in the vertical meridian and an uncorrected or induced vertical imbalance is a frequent source of discomfort and is a resort to aniseikonic explanations, which are often illusory, unless a disparity of over 2 D. in the lenses for the two eyes exists.

In Major Sugar's preferred "reduced" correction of — 2.25 D. sph. ⊃ + 1.00 D. cyl., axis 100 from the — 2.75 D. sph. ⊃ + 2.00 D. cyl., axis 100 estimated by monocular refraction, the reduction of the + 2.00 D. cylinder to a + 1.00 D. cylinder does not affect the vertical heterophoria since the former has no vertical power, although the change of a — 2.75 D. sphere to a — 2.25 D. sphere diminishes the induced vertical heterophoria at the reading level to 0.75 degree of prism base up, an amount which conceivably might be tolerated. Obviously, any increase in comfort obtained by a change in the prescription to — 2.25 D. sph. ⊃ + 1.00 D. cyl., axis 100 could result not from "adjustment" in the optical midpoint but from reduction of the induced vertical heterophoria 50 per cent.

CASE 2.—Private J. D. W., aged 21. Correction was as follows:

Right Eye: — 4.00 D. sph. ⊃ + 2.75 D. cyl., axis 110.

Left Eye: —0.50 D. sph. ⊃ + 1.00 D. cyl., axis 90.

Here, at the reading level, there is an imbalance of 3.5 prism diopters, and a "slabbed-off" prism of 3 diopters base up is needed for the right eye, rather than a reduction in cylinder! The recorrection to — 3.00 D. sph. ⊃ + 1.25 D. cyl., axis 100 reduces the imbalance to 2.25 diopters of

prism base up for the right eye at the reading level, which is still an intolerable amount.

CASE 3.—Private G. W. A., aged 28. Correction was as follows:

Right Eye: + 4.00 D. sph. ⊃ + 1.00 D. cyl., axis 95.

Left Eye: + 3.00 D. sph. ⊃ + 3.25 D. cyl., axis 75.

There are at the reading level a vertical imbalance of 1 degree of prism base up and a lateral imbalance of 1.5 degrees of prism base out. Major Sugar's reduction of this prescription to + 2.25 D. sph. ⊃ + 1.00 D. cyl., axis 95 eliminates one half, but not all, of the prism base out. If the tonic action of the ciliary muscle is allowed for, there is no optical reason why a + 3.25 D. cylinder cannot be tolerated by a patient with hyperopic astigmatism provided that, in a subjective check, the spherical value determined retinoscopically is "fogged" by the addition of a + 0.75 sph. lens and the amount of astigmatism, similarly determined, is checked subjectively and verified by cross cylinder technic for amount and axis.

CASE 4.—Private B. B. I., aged 20. Correction was as follows:

Right Eye: + 1.50 D. sph., axis 90 [sic].

Left Eye: — 2.50 D. sph. ⊃ + 3.50 D. cyl., axis 105.

Again, there is vertical heterophoria of 2 diopters of prism at the reading level, and for the left eye the prescription calls for a "slabbed-off" prism of 2 diopters base up for comfort at the reading level.

In 3 of the 4 cases cited in Major Sugar's interesting paper, a severe vertical induced heterophoria is present at the reading level in an intolerable amount and there obviously would be discomfort. In no case does the author mention the presence of this induced heterophoria at 10 mm. below the optical center, nor does he state that the optician "slabbed off" or dropped the optical centers in the glasses given the patients.

In all 4 cases cited the author resorted to the principle of spherical equivalents (used when monocular or binocular confusion is encountered in the initial use of a high cylinder). It is not understandable how an optician, in grinding these lenses, could fail to "slab off" a prism, or, on the other hand, could fail to grind two pairs of glasses, one with the optical centers coincident with the geometric centers and another, a reading pair, with the optical centers lowered. It seems unnecessary for one to look far afield in seeking an explanation of the discomfort suffered by these patients in binocular vision. One need not postulate either a change in the axis of astigmatism for near vision as compared with that for far vision or invoke the principle of spherical equivalents to reduce the power of the cylinder. Since the indiscriminate cutting of cylinders is a device not to be recommended, it follows that if a patient can accept a high cylinder without confusion in monocular vision and has no induced heterophoria in binocular vision, there is neither physiologic or psychologic reason why he should suffer discomfort. If, however, vertical heterophoria is present at the reading level, this must be eliminated either by "slabbing off" the prism or by some other method, such as decentration, which of course leaves uncorrected prisms base up or base down in the field for distance. Further, if such obvious factors as a dominant or a nondominant eye can be disregarded in the 4 cases cited by Major Sugar, the cause of the discomfort in at least 3 of the 4 cases cited obviously was due to discomfort in near vision, due to an induced, uncorrected and intolerable vertical heterophoria, correctable either by the use of a "slabbed-off" prism (which the patient can easily be educated to use) or by the use of two pairs of glasses, one for distance and one for reading.

HUGH O'NEILL, M.D., Santa Ana, Calif.
2122 North Main Street.

To the Editor:—In the article "Binocular Refraction with Cross Cylinder Technic," in the January issue (ARCH. OPHTH. 31:34, 1944), Major H. Saul Sugar champions the concept of "spherical equivalents" in dealing with anisometropia requiring a refraction in cases of high cylinder correction.

Ordinarily, in the effort to secure minimal blur, the eye with a high cylinder error tends to utilize this device by focusing for the interfocal circle. If the static error is + 2.00 D. cyl., axis 90, the active eye accommodates 1 D. and thus converts its correction to — 1.00 D. sph. ⊃ + 2.00 D. cyl., axis 90. Even with cycloplegia some refractionists not infrequently correct for a confusion disk rather than for a point of focus if their routine is first to determine the sphere that gives the best vision and then to add the weakest acceptable cylinder. On the other hand, refractionists who consider the correct adjustment for astigmatism of paramount import, and who check the correctness of the cylinder by the Lancaster dials before dealing with the spherical correction, are logically less likely to make this error.

In an emmetropic eye the addition of a + 0.50 D. cross cylinder reduces visual acuity of 20/20 to that of 20/25 or 20/30. In the one instance in which Sugar gives the corrected vision before and after application of the "spherical equivalent," the addition of the + 0.50 D. cross cylinder caused this expected reduction in acuity.

Sugar discusses ably the rationale of changes in the power and axis of high cylinders from the cycloplegic to the postcycloplegic state. He fails to explain why, once the correct cylinder

has been determined, it may cause discomfort. In all the cases cited in which the substitution of the "spherical equivalent" made the patient more comfortable, the power in the vertical meridians of the two lenses was made thereby less divergent, and it was simply this reduction in the differential prismatic action of the lenses that accounted for the subjective improvement. The same result can be successfully achieved by other means, such as by incorporation of prismatic compensation in the lower half of one lens, without impairment of the visual acuity of either eye or the sacrifice of binocular vision.

COMMANDER JAMES E. LEBENSOHN (MC), U.S.N.R.

To the Editor:—Commander J. E. Lebensohn, in discussing my recent paper on "Binocular Refraction with Cross Cylinder Technic," points out that the substitution of the "spherical equivalent" made the patient more comfortable simply by the reduction in the differential prismatic action of the lenses. I should like to point out that the subjective examination is carried out with the trial lenses centered before the eyes and the test chart at a distance of 6 meters. Under such circumstances there is no prismatic effect of the lenses. Although the use of prismatic compensation was not under discussion in this particular paper, I should like to indicate here that it is my practice to compensate for vertical prismatic difference at the reading point, but this is done in addition to the use of the "spherical equivalent."

The method used is as follows: The difference in the dioptric value of the two lenses in the 90 degree meridian is multiplied by 0.1 prism diopter per diopter for each 8 mm. of usual vertical displacement, according to Prentice's rule. If the prismatic difference is less than 2 prism diopters, one lens is ground with a lower portion of fused higher index glass to give prism base down in one lens. In plus lenses the prism is applied base down before the more ametropic eye, and in minus lenses, before the less ametropic eye. If the prismatic difference is more than 2 prism diopters, one lens is ground by slab-off technic to give prism base up in one lens. Here the prism is applied to the more ametropic eye in the case of minus lenses and to the less ametropic eye in the case of plus lenses.

MAJOR H. S. SUGAR, Medical Corps, Army of the United States.

Book Reviews

Trabajos publicados en 1942. H. Arruga. Pp. 50, with illustrations. Barcelona, Spain, 1942.

In 1942 Arruga published eight articles, which he has collected in a booklet of fifty pages.

The first article deals with some of the surgical instruments which the author has contributed to ophthalmology. The circular saws, first recommended by Gomez Marquez for perforation of the bone in dacryocystorhinostomy, are again advocated by Arruga. The author's forceps for intracapsular cataract extraction have been modified, with incorporation of features which have been found useful in forceps devised previously by other surgeons. With the original Arruga forceps, in grasping the capsule of the lens, one not infrequently picked up the iris at the same time. In the new forceps this possibility of grasping the iris has been eliminated by rounding the part of the jaws of the forceps which come in contact with the posterior surface of the iris. With the original Arruga forceps, when the capsule of the lens was grasped by the jaws of the forceps, the upper part of the iris was sometimes also grasped by the blades of the forceps, which were in close apposition. In the new forceps the blades are not in apposition anywhere except at the biting jaws, and there is no danger of grasping the iris. A Dimitry type of suction syringe for cataract extraction is also presented.

Arruga has three articles on retinal detachment, two of which repeat what he has maintained in previous publications about the surgical treatment of retinal detachment. In the third article he states that retinal detachment cannot take place unless the retina is altered. The amount of retinal deterioration determines the prognosis—the more pronounced the changes in the retina the worse the prognosis. The formation of a rent in the retina seems, according to the author, to be the chief cause of the production of a retinal detachment. Arruga considers that the framework of the retina is formed by the retinal blood vessels and the fibers of the optic nerve and that this framework determines the shape of the rent.

In the cure of retinal detachment by operation, Arruga states that the membrane which is active in the production of chorioretinal adhesions and

the resorption of the subretinal fluid is the choroid, the retina having only a passive role.

Arruga advocates daily injections of vitamin C after cataract extraction and claims to have obtained a decrease of 20 per cent in the incidence of postoperative hemorrhage with this treatment.

The obliteration of the canaliculi with the galvanocautery had a favorable influence in 5 cases of conjunctivitis sicca.

Color photography of the fundus with the use of the Nordenson apparatus, to which a Zeiss camera is adapted, is described by the author.

In 1 case of absolute glaucoma in which a Lagrange operation was followed by an expulsive hemorrhage, the author practiced an opticociliary neurotomy. With this procedure the hemorrhage was stopped, and the eye was preserved without its becoming atrophic.

Ramón Castroviejo.

The Human Eye in Anatomical Transparencies. Explanatory text by Peter C. Kronfeld, M.D. Anatomical Transparencies by Gladys McHugh. Historical Appendix by Stephen L. Polyak, M.D. Price, $6.50. Pp. 99. Rochester, N. Y.: Bausch & Lomb Press, 1943.

The first part of the book consists of a topographic atlas of the eye and orbit in which a new and elaborate technic is applied to a three dimensional presentation of the gross anatomy of this region. As a result of studies on cadaver preparations and fresh specimens, the artist, Miss Gladys McHugh, presents the anatomic relations in a sequence of 16 instructive colored drawings printed on transparent material. They are taken partly from preparations of anatomic layers and partly from arbitrary dissections of slices of varying thickness. The transparencies are twice the size of the adult eye and represent surface and posterior views of sections on a frontal and on a temporal plane. The diagrammatic simplification is carried out to the irreducible.

The descriptive text accompanying the atlas constitutes the second part of the book and is written by Dr. Peter C. Kronfeld. It is outstanding for teaching purposes as a clear and concise presentation of a complex subject. The small black and white plates illustrating this section of the book are reproductions of the colored plates with the addition of numerous labels. Because of their small size, the number of inscriptions and the lack of contrast, they do not compare well with the text in lucidity. The topographic section is preceded by a brief systematic anatomy of the eye condensed to 35 pages, with 10 large black and white diagrams, and constitutes a modern concept of the fundamentals of ocular anatomy.

The third, and last, part, by Dr. Stephen L. Polyak, will attract the interest of the advanced reader, whereas the first two parts are devoted to the student. The roots of ophthalmology are traced to ancient Greek and Arabian medicine and the subsequent development of early European optics. Black and white reproductions of diagrams taken from ancient literature will appeal to the historical interest of the reader.

Students who do not have the opportunity to perform actual dissections will profit greatly from the use of this book in the study of ocular anatomy. The transparencies will facilitate the understanding of some of the intricate anatomic relations. It is difficult to decide, however, to what extent the study of anatomy can be simplified for the medical student without interference with his active participation in the process of learning.

L. von Sallmann.

Notice

BIELSCHOWSKY'S "LECTURES ON MOTOR ANOMALIES OF THE EYES" AVAILABLE

"Motor Anomalies of the Eyes," by Prof. Alfred Bielschowsky, formerly of the University of Breslau, Germany, and later of Dartmouth Medical School, is now ready for distribution. This book contains four lectures which were delivered by Professor Bielschowsky while he was on the staff at Dartmouth and which were published in the Archives in 1934 and 1935. The book was prepared because of the many requests for reprints of the lectures. It sells for $1.50 postpaid.

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Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

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Place: Oxford, England. Time: July 8-9, 1943.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

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Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.

Place: Rosario. Time: Last Saturday of every month, April to November, inclusive. All correspondence should be addressed to the President.

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Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.

Place: Chicago. Time: June 12-16, 1944.

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President-Elect: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.

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Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.

Place: Hot Springs, Va. Time: May 29-31, 1944.

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President: Dr. R. Evatt Mathers, 34½ Morris St., Halifax, N. S.

Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.

Place: Halifax, N. S. Time: Aug. 4-5, 1944.

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ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.

Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.

Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit. Wis.

Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Paul A. Chandler, 5 Bay State Rd., Boston.

Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.

Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

Pacific Coast Oto-Ophthalmological Society

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

Puget Sound Academy of Ophthalmology and Oto-Laryngology

President: Dr. L. L. McCoy, 1317 Marion St., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

Rock River Valley Eye, Ear, Nose and Throat Society

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

Saginaw Valley Academy of Ophthalmology and Otolaryngology

President: Dr. M. H. Pike, Midland, Mich.
Secretary-Treasurer: Dr. R. H. Criswell, 407 Phoenix Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

Sioux Valley Eye and Ear Academy

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

Southern Medical Association, Section on Eye, Ear, Nose and Throat

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

Southwestern Academy of Eye, Ear, Nose and Throat

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

Southwestern Michigan Triological Society

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave, Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

Western Pennsylvania Eye, Ear, Nose and Throat Society

President: Dr. Ray Parker, 218 Franklin St., Johnston, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg, DuBois.

STATE

Arkansas State Medical Society, Eye, Ear, Nose and Throat Section

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

Colorado Ophthalmological Society

President: Dr. C. A. Ringle, 912–9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer:: Dr. C. K. McLaughlin, 567 Walnut St., Macon.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St, Des Moines.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Val H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St, Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings, Mont.

Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.

Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr B. E. Failing, 31 Lincoln Park, Newark.

Secretary: Dr. George Meyer, 410 Haddon Ave., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. James E. McAskill, 508 Woolworth Bldg., Watertown.

Secretary: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.

Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. T. W. Buckingham, 405 Broadway, Bismarck.

Secretary-Treasurer: Dr. F. L. Wicks, 516-6th St., Valley City.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.

Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.

Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.

Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.

Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.

Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.

Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.

Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. R. B. Maw, 699 E. South Temple, Salt Lake City.

Secretary-Treasurer: Dr. Charles Ruggeri Jr., 1120 Boston Bldg., Salt Lake City.

Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.

Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.

Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.

Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.

Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.

Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.

Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.

Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.

Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.

Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.

Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. William B. Agan, 1 Nevins St., Brooklyn.

Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn.

Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. Walter F. King, 519 Delaware Ave., Buffalo.

Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.

Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.

Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.

Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.

Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago.

Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.

Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.

Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. Shandor Monson, 1621 Euclid Ave., Cleveland.

Secretary: Dr. Carl Ellenberger, 14805 Detroit Ave., Cleveland.

Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.

Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.

Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. H. D. Emswiler, 370 E. Town St., Columbus, Ohio.

Secretary-Treasurer: Dr. D. G. Sanor, 206 E. State St., Columbus, Ohio.

Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. Arthur Padillo, 414 Medical Professional Bldg., Corpus Christi, Texas.

Secretary: Dr. Edgar G. Mathis, 815 Medical Arts Bldg., Corpus Christi, Texas.

Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Abell Hardin, Medical Arts Bldg., Dallas, Texas.

Secretary: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas, Texas.

Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.

Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.

Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Dr. Howell L. Begle, 2730 E. Jefferson Ave., Detroit.

Secretary: Dr. C. W. Lepard, 1025 David Whitney Bldg., Detroit.

Time: 6:30 p. m., first Wednesday of each month, November through April.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.

Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.

Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.

Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.

Time: Third Wednesday in October, November, March, April, May and June.

Eastern Pennsylvania Association of Eye, Ear, Nose and Throat Physicians

President: Dr. James E. Landis, 232 N. 6th St., Reading.

Secretary-Treasurer pro tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.

Time: Last week in April each year.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.

Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.

Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SECTION

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.

Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.

Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

INDIANAPOLIS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.

Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.

Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.

Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.

Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.

Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.

Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. E. Trainor, 523 W. 6th St., Los Angeles.

Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

LOUISVILLE EYE AND EAR SOCIETY

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time. 6:30 p. m., second Thursday of each month from September to May, inclusive.

LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Each member in alphabetical order.

Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Each member in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave, Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. Edwin C. Bach, 324 E. Wisconsin Ave., Milwaukee.

Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.

Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.

Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.

Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

MONTREAL OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.

Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.

Time: Second Thursday of October, December, February and April.

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.

Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashvile, Tenn.

Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.

Secretary: Dr. Frederick A. Wiess, 255 Bradley St, New Haven, Conn.

NEW ORLEANS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.

Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.

Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Frank C. Keil, 660 Madison Ave., New York.

Secretary: Dr. Willis S. Knighton, 121 E. 61st St., New York.

Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President Dr. Sigmund Agatston, 875–5th Ave., New York.

Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.

Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President. Dr. James P. Luton, 117 N. Broadway, Oklahoma City.

Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.

Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President. Dr. D. D. Stonecypher, Nebraska City, Neb.

Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.

Place. Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President. Dr. Thomas Sanfacon, 340 Park Ave, Paterson, N. J.

Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.

Place: Paterson Eye and Ear Infirmary. Time: 9 p. m, last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.

Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.

Time First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr. John B. McMurray, 6 S. Main St., Washington, Pa.

Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.

Place: Pittsburgh Academy of Medicine Bldg. Time Fourth Monday of each month, except June, July, August and September

READING EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. R. M. Brickbauer, Shillington, Pa.

Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading Pa.

Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.

Secretary: Dr. Clifford A. Folkes, Professional Bldg. Richmond, Va.

Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.

Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. C. C. Beisbarth, 3720 Washington Blvd., St. Louis.

Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd., St. Louis.

Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.

Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.

Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.

Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.

Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.

Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.

Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.

Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.

Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.

Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.

Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. E. W. Campbell, 316 Michigan St., Toledo, Ohio.

Secretary: Dr. L. C. Ravin, 316 Michigan St., Toledo, Ohio.

Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.

Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.

Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. S. Bockoven, 1752 Massachusetts Ave., Washington, D. C.

Secretary-Treasurer: Dr. John Lloyd, 1218–16th St. N. W., Washington, D. C.

Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.

Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.

Place: Office of chairman. Time: Last Tuesday of each month from October to May.

ARCHIVES OF OPHTHALMOLOGY

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ACID-BASE TOLERANCE OF THE CORNEA

J. S. FRIEDENWALD, M.D.; W. F. HUGHES JR., M.D., AND H. HERRMANN, M.D.
BALTIMORE

The present investigation is preliminary to a study of the mechanisms by which acids and alkalis damage the cornea. Previous work in this field has been relatively devoid of quantitative analysis. We feel that the prerequisites of a rigorous approach to this problem are: (1) the utilization of isotonic solutions of known p_H composed of simple acids, alkalis or buffer substances; (2) the separation of the physical factors of penetration from those purely chemical effects in which we are primarily interested, and (3) the elaboration of a numerical method of evaluating the severity of the reaction produced, so as to yield data which may be studied statistically and graphically.

METHODS AND MATERIAL

Solutions Used.—In order to have a buffer solution with essentially the same molecular composition over the entire range of p_H studied, we have used the following solution, which is similar to that described by Teorell and Stenhagen:[1] sodium citrate, 0.028 molar; potassium acid phosphate, 0.028 molar; boric acid, 0.028 molar; sodium chloride, 0.083 molar, and sodium hydroxide and hydrochloric acid, in varying amounts to bring about the desired p_H.

This buffer solution varies from a concentration isotonic with a 0.85 per cent solution of sodium chloride to a concentration one and a half times this tonicity. Saline solutions of this molarity do not damage the cornea. The nine dissociation constants of the three trivalent acids in the buffer solution are remarkably well distributed, and the titration curve (fig. 1) correspondingly shows effective buffering capacity over a wide range of p_H. These anions are well tolerated by living tissues, and this buffer solution has, therefore, been highly recommended for physiologic experiments.

For comparison at the extremes of acidity and alkalinity, we have used various dilutions of hydrochloric acid and sodium hydroxide made isotonic by the addition of sodium chloride.

Penetration.—Three series of experiments were performed.

1. Normal rabbit corneas were irrigated with the test solutions for ten minutes. A convenient head holder for rabbits, which allows the use of an ether cone during the experiment, is shown in figure 2. Two small spring clips attached to the upper lid of each eye and linked over the top of the head elevated the lids, and two bulldog clamps hanging on the lower lids exposed the cornea for irrigation. The corneas were kept bathed in the test solution by allowing 1 drop to fall from the buret directly onto the upper portion of the cornea approximately every two seconds.

2. The rabbit corneas were also irrigated after the removal of the corneal epithelium by application of ox bile or a 1 per cent solution of sodium glycocholate, or mechanically by means of a cotton pledget mounted on a toothpick and previously dipped in collodion.[2] As tested with fluorescein, the epithelium was removed most completely by the last method, and no corneal opacification resulted later.

3. One-tenth cubic centimeter of the test solution was injected directly into the corneal stroma with a 25 gage needle and a tuberculin syringe. Ether anesthesia was used in all expermients.

Numerical Methods of Recording Reactions.—The numerical method of quantitative evaluation of the severity of important disease manifestations has been widely used in vitamin studies,[3] having originally been used by Holst and Trøhlich, 1909 to 1910. This method was applied to estimation of the severity of anterior ocular lesions by Rothschild, Friedenwald and Bernstein.[4] It is easy to set up a scale of values for the severity of each symptom: For example, 0 may indicate absence of symptoms; 1, moderately severe symptoms, and 2, extremely severe symptoms. Or 0 may designate absence of symptoms, and 1 may indicate slight, 2 moderately severe, 3 severe and 4 extremely severe symptoms. After a number of lesions of varying degrees of severity have been observed, the major observable signs of the injury and the extreme range of expected variations can be established. Since variations in judgment may lead to moderate discrepancies in the classification of the severity of a single symptom in a given case, the judgment of the severity of the lesion

From the Wilmer Ophthalmological Institute of Johns Hopkins University and Hospital.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Wilmer Ophthalmological Institute of the Johns Hopkins University.

1. Teorell, T., and Stenhagen, E.: Ein Universalpuffer fur den p_H—Bereich 2.0 bis 12.0, Biochem. Ztschr. 299:416, 1938.

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will be less affected by subjective fluctuations if as many symptoms as possible are recorded independently, provided, of course, that the symptoms chosen are significant of the lesions and are not subject to wide inde-

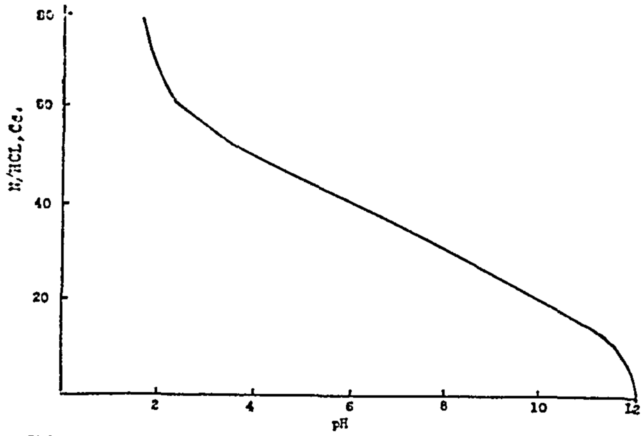

Fig. 1.—Titration curve for a "universal" buffer solution (citrate, phosphate and borate), taken from Teorell and Stenhagen.[1] There is a smooth, gradual change in p_H during titration, indicating effective buffering capacity between p_H 2.0 and p_H 12.0.

Numerical Estimation of the Severity of Lesions Produced in the Cornea of Rabbits' Eyes by Action of Corrosive Agents

Symptom	Maximum Grade, Points
Corneal opacity	
Intensity	8
Area	4
Less than one fourth of cornea = 1	
Less than one half of cornea = 2	
Less than three fourths of cornea = 3	
Over three fourths of cornea = 4	
Duration	4
1 to 3 days = 1	
4 to 6 days = 2	
7 to 13 days = 3	
14 days and over = 4	
Corneal edema or bulge (seen with hand slit lamp and loupe)	4
Corneal slough or ulceration	4
Denuded epithelium = 1	
Moderate slough = 2	
Pronounced slough = 3	
Perforation = 4 (100% lesion)	
Pannus (including density and length)	4
Conjunctiva	
Redness	2
Edema	2
Necrosis	2
Discharge	2
Iritis	4
Small pupil and photophobia = 1	
Congestion of iris or positive aqueous ray = 2	
Exudative iritis = 3	
Panophthalmitis = 4	
	40 × 2.5
	100%

pendent variations from accidental causes, unrelated to the specific experimental lesion. For the present study, the significant symptoms were chosen for grading, and varying maximal values were assigned to them, the rating being dependent on their relative importance (table). The "duration" of the corneal opacity was included only in the final evaluation of a lesion. The ocular lesion exhibiting the most extreme degree of all recorded symptoms on this scale would have a grade of 40 points, and for graphic purposes this maximum lesion is represented as 100 per cent. Since perforation of the cornea represents maximum damage, such a lesion was rated as 100 per cent regardless of whether a lower figure was obtained by a summation of all the symptoms.

It is not to be assumed that a grade of 11 represents a lesion precisely 10 per cent more severe than a lesion with a grade of 10—any more than it is to be assumed that a student who obtains a grade of 90 knows precisely 20 per cent more than a student who has a grade of 75 per cent. Nor is it assumed that the same grade recorded at two different periods of the disease

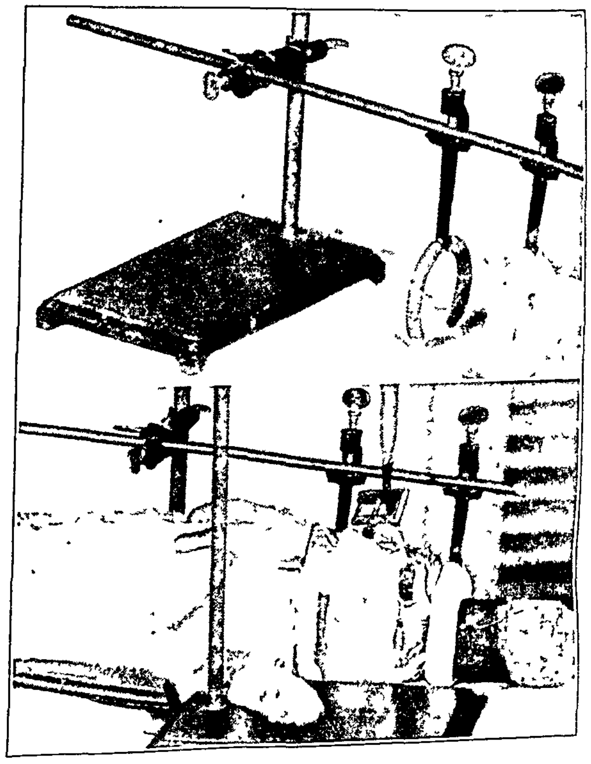

Fig. 2.—Apparatus for holding the rabbit under ether anesthesia during irrigation of the eyes.

indicates an identical condition at those two periods. It is only assumed that, in a comparison of two lesions of the same age, the higher grade is attached to the more severe lesion.

In certain instances of intracorneal injection, irregularly scattered through the series, a peculiar corneal bulge developed which we attributed to accidental trauma, probably a too superficial injection. There appeared less ocular congestion, relatively less corneal opacity and more sharply localized areas of bulging in eyes exhibiting this bulge than in eyes with true corneal edema secondary to a toxic substance. At first values for eyes presenting this phenomenon were omitted from the analysis. Later it was found that if 3 was subtracted from the total score of symptoms for each degree of bulge, the effects of this accidental factor could be

left out of account. The final results are essentially unchanged whether the values for eyes showing this phenomenon are omitted altogether or are included with this correction.

RESULTS

The numerical system of grading lesions outlined here was found to give a useful estimate

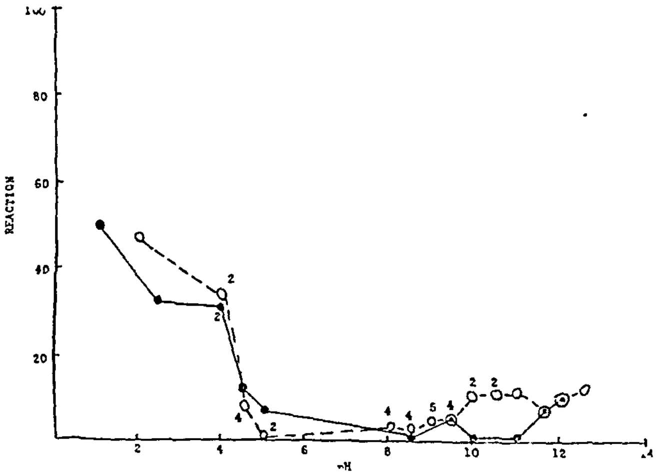

Fig. 3.—Graph showing the close approximation of the severity of the ocular lesions produced by two methods of exposure of the corneal stroma to buffer solutions of varying p_H. In this figure and in the following figures, the number beside each point plotted refers to the number of rabbit eyes tested to obtain the value for that point. The points without numbers represent one experiment.

The values obtained by removal of epithelium followed by irrigation are indicated by the solid line; those by intracorneal injection, by the broken line.

of the severity of lesions in over 400 eyes which had been subjected to various corrosive agents applied in different ways. The grades given by different observers for the same eye were re-

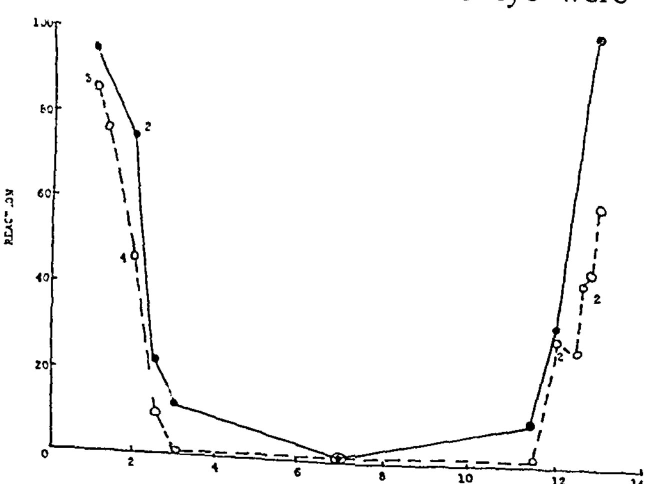

Fig. 4.—Graph showing a less pronounced reaction after intracorneal injection (broken line) of 0.1 cc. of an unbuffered isotonic solution of hydrochloric acid or sodium hydroxide than after continuous irrigation (solid line) of the eye with the same solution with the corneal epithelium removed. This difference in the reactions suggests a buffering capacity of the cornea itself.

markably close. Also, in determination of the lowest concentration of a toxic substance which would produce a corneal lesion, a series of eyes receiving increasing dilutions of the material showed a relatively smooth and proportionate reduction in the numerical grades. Values for the lesions produced by extremes in p_H were consistent.

Two methods for exposure of the corneal stroma to corrosive agents were used in these experiments: mechanical removal of the epithelium with a cotton pledget dipped in collodion followed by irrigation, and the intracorneal injection of 0.1 cc. of the test solution. The results with one method closely paralleled those with the other for the reaction of the eye to buffer solutions over a range of p_H 2.0 to p_H 12.0 (fig. 3). The rabbit cornea will apparently tolerate a solution of p_H 5.0. In several cases in which an alkali burn had resulted in loss of the corneal epithelium in the human eye, irrigation with an isotonic solution of acetate buffer with a p_H 4.7

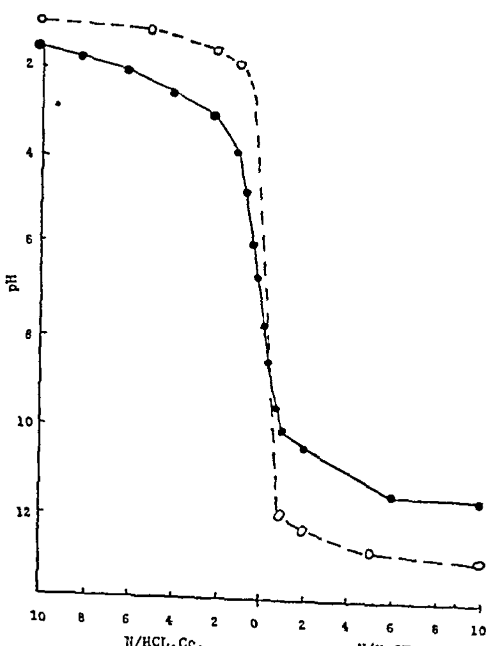

Fig. 5.—Curves for 5 beef corneas (solid line) titrated in a constant volume of 10 cc. of saline solution, a glass electrode being used for determination of the p_H. As compared with the titration curve for hydrochloric acid and sodium hydroxide (broken line), the beef cornea shows buffering capacity.

produced no visible damage. In the alkaline range, buffer solutions with a p_H up to 12.5 produced no severe damage.

Unbuffered isotonic solutions of hydrochloric acid and sodium hydroxide were used to determine the tolerance of the corneal stroma to extremes in p_H (fig. 4). Here it was found that the curves rose sharply at p_H 3.0 and p_H 11.5. It will be noticed that the reactions produced by the intracorneal injections of 0.1 cc. of the isotonic solution of hydrochloric acid or of sodium hydroxide were slightly less than those following irrigation. This suggests that there may be a slight buffering capacity of the corneal substance itself which would neutralize a small

amount of acid or base. Irrigation with large amounts of acid or alkali would overcome such a buffering action.

That the cornea does have a buffering effect was demonstrated by the direct titration of 5 beef corneas in a constant volume of 10 cc. of saline solution, a glass electrode being used for

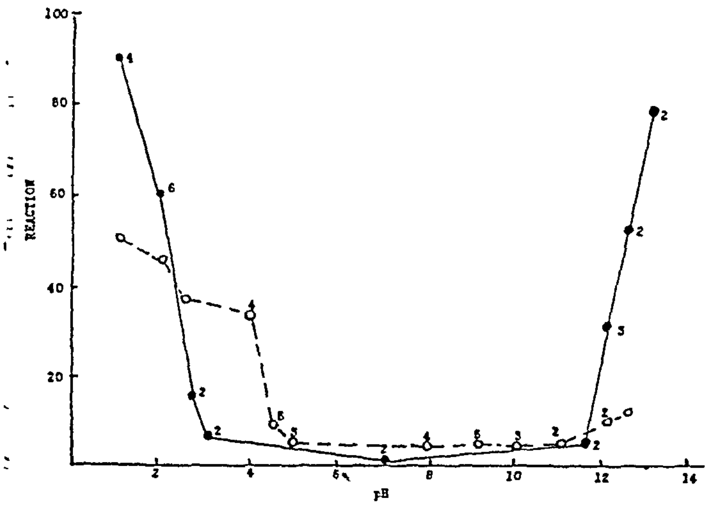

Fig. 6.—Comparison of the reaction curves for buffered (broken line) and for unbuffered (solid line) solutions. The limits of tolerance of the corneal stroma to unbuffered solutions of hydrochloride acid or sodium hydroxide are p_H 3.0 and p_H 11.5 respectively. "Universal" buffer solutions are tolerated only at a p_H above 4.5, an observation suggesting a greater affinity of the trivalent anions for corneal proteins.

the measurement of the p_H (fig. 5). A comparison of the titration curve for the beef cornea with the titration curve for the isotonic solutions of hydrochloride and sodium hydroxide shows some buffering capacity for solutions below p_H 4.0 and those above p_H 10.0. The wet weight of 1 beef cornea is approximately 800 mg., and that of the rabbit cornea is 100 mg. The buffering capacity being assumed to be the same for the two animals, each rabbit cornea will theoretically require the following amounts, expressed in cubic centimeters, of tenth-normal hydrochloric acid or tenth-normal sodium hydroxide, in order that the corneal substance may reach the p_H values indicated:

Acid Range p_H	No. of Cubic Centimeters Required	*Alkaline Range* p_H	No. of Cubic Centimeters Required
4.5	0.08	10.5	0.2
4.0	0.1	11.0	0.5
3.0	0.2	11.5	0.6
2.0	0.8		
1.5	1.0		

If it is assumed that the injected material reaches only one-tenth the corneal stroma, the effective buffering capacity of the cornea would be sufficient to account for the slight difference between the reaction curves produced by irrigation and those by injection of the test solution.

Comparison of the reaction curves of the corneal stroma for buffered and those for unbuffered solutions reveals a difference in their form (fig. 6). At both the acid and the alkaline extreme, the reaction produced by the action of the hydrochloric acid or the sodium hydroxide solution rises sharply outside the limits of p_H 2.5 or p_H 11.5. There is, therefore, a great increase in the corneal reaction for a very small change in p_H at these points. On the other hand, at both extremes in p_H the reaction curve for "universal" buffer solutions is much flatter. The reason for this protective action of the buffer solution is being investigated. From figure 3 it is seen that injection of a buffer solution produces a slightly more severe reaction than irrigation with the solution. This may be due to slow penetration of the large trivalent anions of the buffer.

On the acid side, moreover, reactivity is obtained at a higher p_H with the buffered than with the corresponding unbuffered hydrochloric acid solution, i. e., at p_H 4.5 as compared with p_H 2.5 (fig. 6). The explanation of this discrepancy is also the subject of current study, but it may be suggested that the greater affinity for proteins of the trivalent anions of the buffer solution may account for this difference.

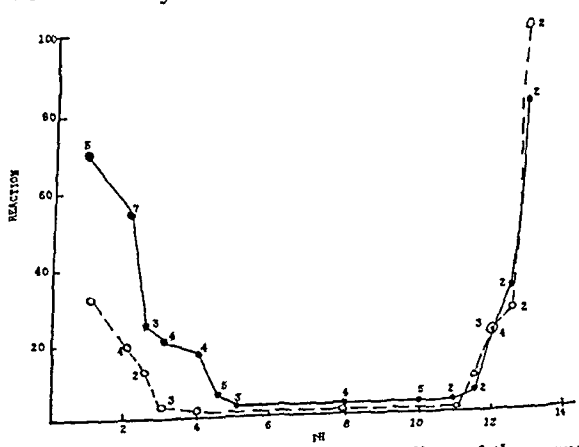

Fig. 7.—Chart showing protective effect of the corneal epithelium against a low p_H. At a high p_H the corneal epithelium is desquamated at the beginning of irrigation, and therefore no difference is found between the curves for simple irrigation and those for intracorneal injection or irrigation after the mechanical removal of epithelium. The values for the stroma are shown by the solid line; those for the intact epithelium by the broken line.

The protective influence of the corneal epithelium is demonstrated by comparison of the effect of irrigations with hydrochloric acid and buffer solution over intact epithelium with the

effect of these solutions when injected intracorneally or when used as irrigations after the mechanical removal of the epithelium (fig. 7). In the acid range this protective influence is pronounced. Application of ox bile or 1 per cent sodium glycocholate produces a diffuse punctate staining of the cornea but does not remove the epithelium completely. Irrigation with acid solutions after the use of bile salts has been found to produce a corneal lesion midway between that of simple irrigation with intact epithelium and irrigation after the complete removal of the epithelium by mechanical means. On the other hand, one of the first effects of irrigation with solutions of sodium hydroxide is swelling and desquamation of the epithelium. Hence the preliminary removal of the epithelium has less effect on the intensity of alkali burns.

SUMMARY

The applicability of the scale of grading the severity of corneal lesions produced by acids and alkalis has been demonstrated. The only important barrier to penetration of the substances used is the corneal epithelium. With buffer solutions and with isotonic solutions of hydrochloric acid or sodium hydroxide, it is possible to study the p_H tolerance of the cornea, but this is found to be not wholly independent of the ionic species used.

The Wilmer Ophthalmological Institute of Johns Hopkins University.

MENINGOCOCCIC CONJUNCTIVITIS

A. B. MANGIARACINE, B.A., AND ABRAHAM POLLEN, M.D.
BOSTON

Although meningococcic conjunctivitis has long been recognized as a complication of cerebrospinal meningitis, its incidence has diminished notably in recent years with the introduction of antimeningococcic serum therapy. Thus, Randolph,[1] in 1893, cited Hirsch, Ziemssen and Hess as finding it an invariable concomitant of the cerebral disease. But, with the advent of serum therapy, no conjunctivitis occurred in a series of 66 cases reported by Lewis [2] in 1931 and was present in only 1 of a large number of cases reported by Tillet and Brown [3] in 1935. Cushing,[4] in 1940, was able to demonstrate only 4 instances of conjunctivitis among 124 cases of cerebrospinal meningitis.

Acute meningococcic conjunctivitis without any other clinical evidence of meningitis, or its development prior to the onset of meningitis, however, is not common at all, there being only infrequent reports of such an occurrence in the literature. Koplik,[5] in 1904, in a report of 77 cases of cerebrospinal fever, described only 1 case in which there was a history of conjunctivitis prior to the onset of meningeal symptoms, and Smith,[6] in 1905, reported another case of meningococcic conjunctivitis in a patient exposed to epidemic meningitis. McKee,[7] in 1908, posed the question as to whether the conjunctiva itself is an independent site of entry for meningococci or whether their presence there is secondary to that of similar organisms in the nose and throat, and in 1909 the same investigator [8] isolated the organism from the bacterial flora of a normal eye. Gifford and Day [9] reported a single case of meningococcic conjunctivitis without any other systemic manifestations, and Reese [10] described a case of conjunctivitis of meningococcic origin followed by meningococcic septicemia and abortive meningitis. Hayden and Hayden [11] reported single cases of meningococcic conjunctivitis occurring in one eye only and observed that the degree or course of the infection in their cases was not as severe as is commonly noted with gonorrheal conjunctivitis. This observation was confirmed by Clifton and Laird,[12] who described 2 cases of acute conjunctivitis of meningococcic origin unassociated with any other meningeal symptoms. In a report on meningococcic infection in soldiers, Daniels and associates,[13] in September 1943, studied 112 cases and mentioned as complications of the disease the occurrence of transient paralysis of the sixth nerve in 3 and of corneal ulcer in 1. In a similar report, made at the same time, Hill and Lever,[14] who studied 68 cases of meningococcic infection in soldiers, mentioned as complications transient paresis of ocular muscles in 50. In neither of these reports, however, was there any case in which meningococcic conjunctivitis occurred prior to the onset of meningeal symptoms.

The occurrence of meningococcic conjunctivitis is obviously of the utmost epidemiologic significance, and the following 10 cases, therefore, are all unusual in that they represent known

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11. Hayden, A. F., and Hayden, A. F.: Acute Conjunctivitis Caused by Gram-Negative Diplococcus Resembling Gonococcus, Brit. J. Ven. Dis. **15**:45, 1939.

12. Clifton, F., and Laird, S. M.: Acute Meningococcal Conjunctivitis, J. Roy. Army M. Corps **77**:318, 1941.

13. Daniels, W. B.; Solomon, S., and Jaquette, W. A., Jr.: Meningococcic Infection in Soldiers, J. A. M. A. **123**:1 (Sept. 4) 1943.

14. Hill, L. W., and Lever, H. S.: Meningococcic Infection in an Army Camp, J. A. M. A. **123**:9 (Sept. 4) 1943.

instances of acute suppurative conjunctivitis of meningococcic origin.

REPORT OF CASES

CASE 1.—J. S., aged 14 weeks, was admitted to the hospital with edema and redness of the left eye of three days' duration, their onset being followed twenty-four hours later by a purulent discharge. Two days later the right eye became similarly involved. The patient had had a "cold" nine days prior to appearance of the ocular symptoms and was treated by a local physician, with subsidence of symptoms in two days. The past and family histories were noncontributory.

Examination on admission to the hospital revealed edema of the upper and lower lids of both eyes, with moderate conjunctival and pericorneal injection. Both eyes showed a moderate purulent discharge, but the corneas were clear. No general systemic symptoms or signs were present.

Smears taken from both eyes on the day of admission revealed the presence of many gram-negative intracellular diplococci, which on culture proved to be meningococci.

The patient was given sulfadiazine orally and placed under a regimen of irrigation of both eyes with a saturated solution of sulfanilamide followed by instillation of a 5 per cent sulfathiazole ointment.[14a] The swelling, redness and discharge gradually subsided, and the patient was discharged seven days after admission, with the process in both eyes quiescent and the appearance normal.

A follow-up examination in the clinic one week later revealed no pathologic signs referable to the eyes.

CASE 2.—A. D., aged 2 years, entered the hospital with a purulent discharge from the right eye for two days, followed one day later by the onset of discharge from the left eye. Smears taken at another hospital were said to reveal the presence of gram-negative intracellular diplococci. No other local or systemic symptoms were noted. The past and family histories were without significance.

Examination revealed some redness of the lids of the right eye, with profuse purulent discharge. The conjunctiva and pericorneal region were moderately injected. There was a slight purulent discharge from the left eye. The corneas of the eyes were clear. Examination, both local and general, revealed nothing else of significance.

Smears taken on the day of admission revealed gram-negative intracellular diplococci, which on culture proved to be meningococci.

The patient was given local therapy only, consisting of irrigations with a saturated solution of sulfanilamide followed by instillation of a 5 per cent sulfathiazole ointment. The redness and discharge gradually subsided; smears became negative, and the patient was discharged five days after admission.

A follow-up examination in the ophthalmic clinic one week later revealed that both eyes were normal.

CASE 3.—F. M., a youth aged 15 years, was admitted to the hospital with a history of edema and redness of the left eye, with suppurative discharge, for three days. Six days prior to admission he was said to have had a "cold," manifested by malaise and a serous discharge from the nose, the symptoms subsiding rapidly. The past and family histories were noncontributory.

Examination revealed moderate edema of the lids of the left eye, with pronounced conjunctival injection and profuse purulent discharge. There was edema of the epithelium, but no ulceration. The right eye was normal. The results of local examination were otherwise normal, and the general physical condition was good.

Smears of material from the left eye revealed many gram-negative intracellular diplococci, which on culture proved to be meningococci type I. The left eye was given local treatment, consisting of atropine and irrigations with a saturated solution of sulfanilamide followed by instillation of 5 per cent sulfathiazole ointment.

On the evening of the day of admission the patient complained of headache, malaise and nausea, with gradual elevation of temperature to 105.8 F. There were no signs of meningeal irritation at this time. By the following morning, however, the patient presented the clinical picture of meningitis, with stiffness of the neck, a bilateral Kernig sign and numerous petechiae scattered over the trunk and extremities. The heart, lungs and abdomen were normal. Lumbar puncture revealed elevated pressure; the fluid was cloudy and contained 984 cells per cubic millimeter, 94 per cent of which were polymorphonuclear leukocytes. A smear showed no bacteria. The white blood cell count was 33,000, with 92 per cent polymorphonuclear leukocytes.

Sulfadiazine was given intravenously, but its administration was followed in a few hours by the development of hematuria, and chemotherapy was discontinued. The temperature had meanwhile dropped to normal. Culture of material from the left eye and of the cerebrospinal fluid revealed a type I meningococcus. Treatment with intravenous injections of antimeningococcic horse serum and small intramuscular doses was started. Under this regimen, the temperature on the second day gradually rose to 102.5 F. and thereafter fell to normal, remaining so throughout the rest of the patient's stay in the hospital. A blood culture made two weeks later showed no growth, and lumbar puncture on the eighth day in the hospital yielded normal fluid. The course thereafter was uneventful, and the patient was discharged on the sixteenth day.

The left eye gradually improved during this period, becoming almost entirely clear six days after admission to the hospital. When it was examined at the time of the patient's discharge, the eye showed nothing abnormal.

CASE 4.—J. H., a boy aged 11 years, was admitted to the hospital with redness, swelling and photophobia of both eyes of four days' duration, the onset being followed one day later by a profuse purulent discharge. About six days prior to admission he was said to have had a mild infection of the upper respiratory tract. No other local and no general symptoms were noted. The past and family histories were noncontributory.

Examination revealed edema of the lids of both eyes, with pronounced conjunctival and pericorneal injection and profuse purulent discharge. Both corneas were steamy and displayed small superficial ulcers. Smears of material from both eyes revealed many gram-negative intracellular diplococci, which were shown on culture to be meningococci type I. The rest of the ocular, as well as the general, examination revealed nothing significant. The patient was placed under treatment, consisting of atropine and irrigations of a saturated solution of sulfanilamide followed by instillation of 5 per cent sulfathiazole ointment.

On the morning after admission the patient's temperature suddenly rose to 104.5 F., and he complained of malaise, nausea, chilly sensations and severe frontal headache. There were no signs of meningeal irritation, and physical examination revealed essentially a normal

14a. Five per cent sulfathiazole in a tragacanth-glycerin base.

condition except for the presence of a diffuse petechial rash over the trunk and extremities. The white cell count was 13,800, with 73 per cent polymorphonuclear leukocytes. A spinal puncture performed at this time revealed nothing of significance. The blood culture and culture of material from the throat, however, both yielded type I meningococci.

The patient was given sulfadiazine immediately, both intravenously and orally. Within twelve hours the temperature dropped to normal, remaining so for the rest of his stay in the hospital. His symptoms gradually subsided, and no meningeal signs developed. The corneal ulcers in both eyes gradually faded into superficial nebulas, and repeated smears were negative for bacteria. The patient had an uneventful convalescence and was discharged on the thirteenth day in the hospital. Ocular examination in the ophthalmic clinic one week later showed an essentially normal condition except for a faint central nebula in each eye.

Case 5.—V. S., aged 13 years, entered the ophthalmic clinic with a history of redness and purulent discharge for four days, which started in the right eye and was followed three days later by similar involvement of the left eye. There were no prodromal disturbances and no systemic symptoms. The rest of the history was noncontributory.

Examination displayed considerable conjunctival injection in both eyes, with profuse purulent discharge. The corneas of both eyes were clear, and the rest of the ocular examination revealed nothing abnormal. Smears displayed the presence of many gram-negative diplococci, and culture revealed a pure growth of meningococci type II.

The patient refused to go to the hospital and was sent home, with instructions to use simple irrigations of a solution of zinc sulfate. The redness and discharge gradually subsided, disappearing entirely in a week. When the patient was seen in the ophthalmic clinic, about three weeks later, there were no abnormal ocular signs.

Case 6.—R. H., aged 10 years, was admitted to the hospital with a history of swelling, redness and photophobia of the right eye, with purulent discharge, the appearance of symptoms being followed one day later by similar involvement of the left eye. There were no other local and no systemic symptoms. The past and family histories were noncontributory.

Examination revealed moderate edema of the lids of both eyes, with pronounced conjunctival and pericorneal injection and profuse purulent discharge. Both corneas displayed a faint central superficial nebula but no ulceration. Smears were positive for gram-negative intracellular and extracellular diplococci, and culture yielded a growth of meningococci type I. The rest of the ocular, as well as the general physical, examination revealed nothing significant.

The patient was given local therapy only, consisting of irrigations with a saturated solution of sulfanilamide followed by instillation of 5 per cent sulfathiazole ointment and atropine. The redness and discharge gradually subsided, and smears became negative for the diplococci. The patient was discharged on the tenth day in the hospital, with no abnormal signs except for the faint corneal nebulas, centrally situated in each eye.

When the patient was seen in the ophthalmic clinic one week later, the process in both eyes was quiescent, and there were no abnormal signs.

Case 7.—R. K., aged 6 years, was admitted to the hospital with a history of swelling and redness, with purulent discharge, in both eyes of one day's duration, the symptoms starting in the right eye and passing a few hours later to the left eye. No other symptoms, local or general, were noted. The past and family histories were noncontributory.

On examination, both eyes displayed pronounced conjunctival injection, with palpebral edema and profuse purulent discharge. The cornea of the right eye revealed a small, superficial central ulceration, and the cornea of the left eye, a central nebula with surrounding edema. Smears of material from each eye showed many extracellular and some intracellular gram-negative diplococci. Culture revealed meningococci type II. The rest of the ocular, as well as the general, examination revealed nothing abnormal.

Local and general therapy was instituted, consisting of irrigations with a saturated solution of sulfanilamide followed by instillation of a 5 per cent sulfathiazole ointment and atropine and oral administration of sulfadiazine. The corneal ulcer in the right eye gradually faded to a tiny superficial nebula, and the injection of and discharge from both eyes gradually subsided. On discharge from the hospital, ten days after admission, both eyes were normal except for faint central nebulas. Repeated smears were negative for bacteria.

When the patient was seen in the ophthalmic clinic, two weeks after discharge, both eyes appeared normal.

Case 8.—C. R., a boy aged 11 years, entered the hospital with a history of purulent discharge from the right eye for four days, accompanied by redness, swelling and photophobia. He stated that about one hour prior to the onset of symptoms a "piece of dust had been removed" from the right eye. One day prior to the onset of ocular complaints a "cold," manifested by nasal discharge and occasional sneezing, had developed. There were no other symptoms. The past history was interesting in that about eight months before he had been admitted to the hospital with a diagnosis of bilateral optic neuritis, followed by optic nerve atrophy. No cause for this condition was ever discovered, in spite of an extensive study of the case. The family history was noncontributory.

Examination on admission revealed edema of the upper and lower lids of the right eye, with pronounced conjunctival and pericorneal injection. There was a profuse purulent discharge. The cornea was clear. The fundi of both eyes showed optic nerve atrophy. The left eye was otherwise normal. Except for slight coryza, the general physical condition was normal.

Smears taken on the day of admission revealed the presence of many gram-negative intracellular diplococci, and meningococci type I were cultured. The patient was placed under local therapy only, which consisted of irrigations with a saturated solution of sulfanilamide followed by instillation of a 5 per cent sulfathiazole ointment.

The discharge ceased three days after admission, and injection gradually subsided. Repeated smears were negative for bacteria. The patient was discharged one week after admission, at which time there were no abnormal ocular signs except for the long-standing optic nerve atrophy.

Case 9.—W. H., a boy aged 11 years, entered the hospital with a history of purulent discharge from the right eye for three days, accompanied by redness, photophobia and occasional pain. He stated that one day prior to the onset of the ocular symptoms he had been "struck in the right eye by a football." There were no prodromal symptoms, and the family and past histories were essentially noncontributory.

Examination on admission revealed edema of the lids of the right eye, with moderate purulent discharge and pronounced conjunctival and pericorneal injection. There were numerous petechial subconjunctival hemorrhages, apparently secondary to the trauma sustained by the eye. The cornea was edematous but displayed no ulceration. There were a congenital defect of the iris and a congenital cortical cataract, confined to the segment of the eye corresponding to 11 o'clock. The ocular, as well as the general physical, examination revealed nothing else abnormal.

Smears taken on the day of admission revealed many gram-negative intracellular diplococci, from which meningococci type I were cultured.

The patient was given local therapy, consisting of irrigations with saturated solution of sulfanilamide followed by instillation of 5 per cent sulfathiazole ointment. The discharge cleared two days after admission and the edema and injection of the cornea and the subconjunctival hemorrhages gradually disappeared. The patient was discharged one week after admission, at which time there were no abnormal ocular signs except for the congenital defects.

Case 10.—T. C., aged 7 months, was admitted with a history of discharge from the left eye, accompanied by redness and swelling, for three days. His mother noticed a slight improvement in the condition of the eye during the twenty-four hours before admission but definite signs of a "cold."

Examination of the left eye revealed deep injection of the conjunctiva and a purulent discharge. The right eye was normal. Smears revealed many gram-negative intracellular and extracellular diplococci.

General examination revealed essentially a normal condition. The temperature was 100.4 F. on admission. Cultures of material taken from the left eye and from the pharynx on admission revealed large numbers of type I meningococci.

The patient was given treatment for the eyes, consisting of irrigations with a saturated solution of sulfanilamide followed by instillation of 5 per cent sulfathiazole ointment.

Two days after admission the temperature became elevated to 100.8 F. The patient appeared somewhat groggy and hoarse. He refused food but took fluids well. Examination at this time revealed a slight discharge from the left eye and nose, slight coryza and inflammation of the pharynx; there were no petechiae and no Kernig sign. The spinal fluid taken at this time was normal. The white blood cell count was 13,950, with 55 per cent polymorphonuclear leukocytes.

In view of the bacteria present in secretions from the eye and pharynx, the boy was given sulfadiazine orally. The temperature remained elevated for two days longer, after which it dropped to normal and remained so for the rest of his stay in the hospital.

A culture of material from the pharynx taken two days before discharge was negative for meningococci. Smears and cultures of secretions from the left eye were also negative, and both eyes appeared normal on examination.

It is interesting to note that the mother became ill with a bad "cold" two days after the patient's admission to the hospital. Cultures of material taken from her pharynx at this time showed large numbers of type I meningococci.

BACTERIOLOGIC STUDY

Differential cultures were made in all the present cases and were directed especially toward the identification of gonococci and meningococci. The organisms were grown on (1) Mueller's starch [15] agar, in which gonococci grow especially well, and (2) Difco chocolate agar, prepared from Bacto Proteose no. 3 agar, which is particularly favorable to the growth of meningococci. Each medium had been recently prepared, and care was taken to be sure they had not dried out.

The plates were incubated in an atmosphere containing approximately 10 per cent carbon dioxide immediately after inoculation. The carbon dioxide atmosphere was obtained by burning a smokeless lighted candle in a sealed jar. The growth was often evident in twenty-four hours, but the culture was not considered negative for the bacteria until after incubation of at least forty-eight hours.

In instances in which the original culture was not pure, single colonies were transferred onto fresh plates. Transplants were then made from these pure cultures onto carbohydrate mediums and differentiated from other gram-negative cocci according to the usual procedure.

SUMMARY AND COMMENT

The 10 cases of acute suppurative conjunctivitis of meningococcic origin described here all occurred within a five month period (May to September 1943), and in none of them, as far as could be determined, was there any definite history of exposure or general prodromal symptoms. In 5 of the 10 cases the patient was said to have had a "cold" at some time prior to or at the time of the onset of the ocular infection, but this seemed to bear no definite relation either to the onset or to the course of the ocular symptoms.

The ages varied from 14 weeks to 15 years, and all the patients were males.

Of the 10 cases, frank meningitis (type 1) developed in 1, and meningococcic septicemia (type 1) with abortive meningitis, in another. Cultures of material from the eyes yielded type 1 meningococci in 4 other cases and type II meningococci in 2 cases. In the first 2 cases the organism was not typed.

Both eyes were involved in 6 cases and one eye only in 4 cases.

There was corneal involvement in 5 of the 10 cases, superficial ulcers developing in 2 cases and corneal edema alone in 3 cases. In *none* did a permanent residual ocular change follow therapy.

Treatment consisted of local and oral chemotherapy in 5 instances. Four patients received

15. Mueller, J. H., and Hinton, J.: A Protein-Free Medium for Primary Isolation of the Gonococcus and Meningococcus, Proc. Soc. Exper. Biol. & Med. **48:**330 1942.

local chemotherapy only, and 1, irrigations with zinc sulfate alone. The oral chemotherapy was given only in cases in which corneal involvement or systemic or meningeal symptoms were present. On the whole, neither the degree nor the course of the ocular infection seemed to be improved by the addition of oral administration of sulfadiazine, and the patient who received zinc sulfate alone did as well as the rest.

The average length of hospitalization (exclusive of the cases with meningeal involvement) was eight days, the ocular discharge subsiding in three to five days and the eyes becoming white and the process quiescent in seven days.

The apparent recent increase in the incidence of cases of suppurative conjunctivitis of meningococcic origin, previously considered of infrequent occurrence, leads one to believe that previous cases may have been missed because of the morphologic resemblance of the organisms to those in the neisserian group. The demonstration of gram-negative intracellular diplococci in the smear of a patient with acute suppurative conjunctivitis usually prompts one to suspect a gonorrheal infection. Differential cultures, however, will easily lead to the correct diagnosis—a factor of great importance when one is dealing with an organism of such potential epidemic virulence as the meningococcus.

NOTE.—Since the presentation of this paper for publication, a new case of meningococcic conjunctivitis has been reported by Reid and Bronstein,[16] and we have studied an additional case. In the latter the condition was limited to one eye and was due to the meningococcus type II. This organism was also cultured from material from the patient's pharynx.

243 Charles Street.

16. Reid, R. D., and Bronstein, L. H.: Meningococcic Conjunctivitis, J. A. M. A. **124**:704 (March 11) 1944.

DI-N-BUTYLCARBAMINOYLCHOLINE SULFATE

A NEW CYCLOPLEGIC AND MYDRIATIC DRUG

KENNETH C. SWAN, M.D., AND NORMAN G. WHITE, M.S.

IOWA CITY

Carbaminoylcholine chloride (doryl) does not affect the surface tension of water. Recently, we have synthesized surface-active derivatives of this compound by replacing the hydrophilic NH_2 group with water-insoluble amines, e. g., di-n-butylamine (fig. 1). This change in molecular structure and surface activity reverses the effects of the drug on the intraocular muscles. While the effects of carbaminoylcholine chloride simulate those of stimulation of the parasympathetic

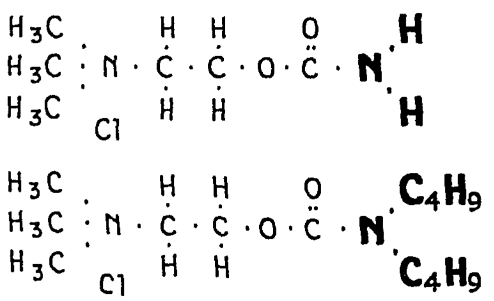

Fig. 1.—*A,* carbaminoylcholine chloride, and *B,* di-n-butylcarbaminoylcholine chloride.

nerves, i. e., miosis and cyclotonia, the action of the new surface-active derivatives simulates that of paresis of the parasympathetic nerves, i. e., mydriasis and cycloplegia. Synthesis and preliminary studies of the pharmacologic action of the new drugs on the eyes have been reported previously.[1] A more detailed investigation of the new class of drugs is the basis of this report.

It was our purpose to synthesize an improved cycloplegic and mydriatic drug for use in routine refraction and internal examination. For this purpose the tropine derivatives, i. e., atropine, homatropine and scopolamine, have many disadvantages, but there have been no substitutes. Ideally, the new drug should be readily available, inexpensive and chemically stable. It should have bactericidal properties, so that solutions would not require sterilization or addition of preservatives. Solutions should be nonirritating and effectively absorbed from the conjunctival sac. The dose producing maximal ocular effects by local application should be several times less than that required to produce minimal systemic reactions. Side effects on the eye, such as vasodilation, increased intraocular pressure and anesthesia, should be negligible. The drug should be nontoxic in therapeutic doses, its pharmacologic action consistent and its idiosyncrasies rare. Finally, the duration of action of the new drug should be short, so that patients will not have prolonged periods of visual disability as a result of ocular examinations. Of the new choline esters synthesized, di-n-butylcarbaminoylcholine sulfate most nearly meets these ideal requirements (fig. 2.).

Di-n-butylcarbaminoylcholine sulfate occurs as white, slightly hygroscopic crystals. It is practically odorless but has a bitter taste. The drug is synthesized by a relatively simple method from inexpensive and readily available chemicals. Dissolved in distilled water and kept in alkaline-free, dark glass bottles, it is stable at room temperature for weeks. Heat and light result in slow decomposition. As decomposition is usually associated with a shift in the hydrogen ion concentration from the acid to the alkaline side, it can be detected with litmus paper. Partially decomposed solutions become slightly irritating but are not toxic to the ocular tissues. A 7.5 per cent solution in distilled water is slightly acid and has

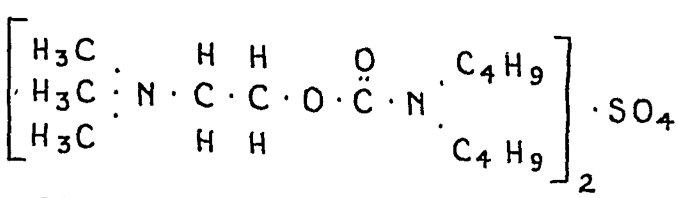

Fig. 2.—Di-n-butylcarbaminoylcholine sulfate.

an air-water interfacial tension of slightly less than 48 dynes per cubic centimeter at 25 C. Alkalis facilitate decomposure, but the new drug does not have the considerable chemical incompatibilities of the tropine alkaloids.

Solutions containing less than 4 per cent of the drug are bland, and concentrations of 4 to 7.5 per cent are only slightly irritating to the normal conjunctiva. Repeated instillations of 5 to 7 per cent solutions into the conjunctival sac may

From the Department of Ophthalmology, State University of Iowa College of Medicine.

This investigation is part of a study being conducted under a grant from the John and Mary R. Markle Foundation.

1. Swan, K. C., and White, N. G.: Some Choline Esters with Cycloplegic and Mydriatic Action, Proc. Soc. Exper. Biol. & Med. **53**:164-166 (June) 1943.

create a transitory punctate disturbance in the epithelium, similar to that produced by other surface-active drugs, e. g., zephiran chloride.[2] These lesions rarely occur after the one or two instillations which are usually required for routine examination. They are perceptible only on biomicroscopic examination with the slit lamp and do not interfere with refraction or ophthalmoscopic examination.

Five per cent solutions of the chloride and the sulfate salt of di-n-butylcarbaminoylcholine were instilled two or three times daily into the conjunctival sacs of rabbits for one to three months. No evidences of injury to the intraocular tissues other than the epithelial changes already described were noted on biomicroscopic examination with the slit lamp or on ophthalmoscopic or histologic study.

A satisfactory chemical method of analysis of the ocular tissues for the drug has not been found; however, penetration of the cornea by the new drug seems to be consistent, as judged by the onset, intensity and duration of mydriasis and cycloplegia. In this respect the new drug differs from the related surface-inactive compound carbaminoylcholine. The latter penetrates the normal epithelium poorly.[3]

Experimental evidence indicates that the new drug produces mydriasis by paresis of the sphincter of the iris (atropine-like action), rather than by stimulation of the dilator fibers (epinephrine-like action). In the rabbit the mydriasis produced by the new drug is submaximal but becomes maximal on electrical stimulation of the cervical sympathetic nerves; therefore, the dilator fibers of the iris cannot have been stimulated effectively by the drug. In contrast, the drug blocks reactivity of the pupil to electrical stimulation of the oculomotor nerve; i. e., the drug has produced paralysis of the sphincter muscle. These experiments do not exclude the possibility that the drug has some effect on the dilator muscles; rather, they indicate that the predominant action of the drug is on the sphincter.

It is probable that the action of di-n-butylcarbaminoylcholine on the iris is the same in human subjects as in rabbits, causing paresis of the sphincter. The mydriasis produced by the new drug is submaximal and is increased by administration of epinephrine, which stimulates the dilator fibers but is unaffected by administration of atropine. The latter, like the new drug, produces paralysis of the sphincter. Cycloplegia produced in the human eye by the new drug simulates the cycloplegia produced by paresis of the oculomotor nerve.

The exact site of action of di-n-butylcarbaminoylcholine has not been established definitely; however, it is probable that the drug acts directly on the muscle cells, for it reduces reactivity of the sphincter of the iris to direct electrical stimulation, as well as to electrical stimulation of the oculomotor nerve. The action of di-n-butylcarbaminoylcholine on the intraocular muscles is antagonistic to that of pilocarpine, physostigmine and acetylcholine, but in combination with physostigmine it produces paresis of skeletal muscle in rabbits. Additional studies will be required to determine whether the new drug acts synergistically with atropine or other tropine derivatives. Cycloplegia produced by the new drug is not noticeably enhanced by paredrine hydrobromide, but mydriasis is increased.

Di-n-butylcarbaminoylcholine has been administered to the eyes of more than 700 patients over a period of a year and a half. One drop of a 7.5 per cent aqueous solution of the sulfate salt instilled into the conjunctival sac produced mydriasis and cycloplegia beginning in from twenty to thirty minutes and becoming maximal in fifty to seventy minutes. In contrast to the action of the tropine derivatives, in which maximal mydriasis and complete loss of the pupillary light reflex considerably precede and outlast maximal cycloplegia, mydriasis and cycloplegia produced by the new drug develop and wear off simultaneously.

The effects of the new drugs on the intraocular muscles remain maximal for approximately two to three hours, after which the effects wear off gradually. Seven to twelve hours after a single instillation the intraocular muscles usually react normally. With two instillations at ten to fifteen minute intervals the duration is several hours longer. In contrast, the cycloplegia, and particularly the mydriasis, produced by a single instillation of a 5 to 7.5 per cent solution of homatropine hydrochloride last considerably longer. The average emmetropic young adult receiving homatropine is able to read in eight to fourteen hours, but the visual near point does not return to normal for twenty to twenty-four hours. The pupil and pupillary reflexes usually do not return to normal for thirty-six to forty-eight hours.

The intensity of cycloplegia and mydriasis produced by a 7.5 per cent solution of di-n-butylcarbaminoylcholine sulfate was found to be equivalent to that produced by 5 per cent homatropine hydrochloride. A group of 74 young adults had refractions both with the new drug and with homatropine. The 148 eyes required an average

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2. Swan, K. C.: Advances in the Medical Treatment of Glaucoma, Journal-Lancet **62**:79-82 (March) 1942.

3. O'Brien, C. S., and Swan, K. C.: Carbaminoylcholine Chloride in the Treatment of Glaucoma Simplex, Arch. Ophth. **27**:253-263 (Feb.) 1942.

of 0.04 D. less plus sphere with the new drug than with homatropine. The difference in the astigmatic correction was also insignificant. Minimal residual accommodation was determined by adding a + 3 D. sphere to the cycloplegic correction and determining the range over which the patient could read 0.5 print in good illumination. Residual accommodation, ranging from 0.6 to 1.5 D., was found with both drugs when single instillations were made and repeated in ten minutes.

Most patients found solutions of 5 per cent homatropine hydrochloride and 7.5 per cent di-n-butylcarbaminoylcholine sulfate to be about equally irritating; however, congestion of the conjunctival vessels was much more pronounced in the eyes receiving homatropine.

The new drug was not found to influence the intraocular tension of 50 normal adults, varying in age from 24 to 78 years; however, the drug produced a *rise in intraocular pressure in* 3 patients with suspected glaucoma simplex. The average maximal rise in tension produced by single instillations of a 7.5 per cent solution was 5.4 mm. Schiøtz, as compared with an average rise of 8.3 mm. produced by single instillations of 5 per cent homatropine hydrochloride. The rise in intraocular pressure lasted an average of nine and a half hours with the new drug, as compared with twenty-three hours with homatropine. It appears, then, that there is less danger of the creation of a rise of intraocular pressure with the new drug than with homatropine.

Di-n-butylcarbaminoylcholine sulfate has antiseptic properties which are lacking in the tropine derivatives. The new drug in concentrations of 0.1 to 0.3 per cent inhibits the growth of strains of staphylococci, pneumococci and alpha hemolytic streptococci isolated in cases of ocular infections. Concentrations of 0.5 per cent promptly sterilize twenty-four hour broth cultures of the same organisms.

The systemic pharmacologic effects of the new drug will be reported on separately; however, it is noteworthy that even in young children systemic symptoms are negligible after instillations of a 7.5 per cent solution into the conjunctival sac. The dry mouth, flushed skin, excitation of the central nervous system and depression which limit the dose of the tropine derivatives do not occur after instillations of the new drug into the conjunctival sac.

The pharmacologic action of di-n-butylcarbaminoylcholine sulfate is as consistent as that of the tropine derivatives. No idiosyncrasies to the drug have been noted in the 700 patients who have received the drug.

No allergic reactions of the conjunctiva or the skin of the lids of the "contact" type have been observed. The series of 700 patients is too small to be conclusive; however, it is noteworthy that contact dermatitis and conjunctivitis resulting from carbaminoylcholine or other choline esters have never been recorded, while contact dermatitis with tropine derivatives, particularly atropine, is not uncommon.

COMMENT

Clinical investigation of di-n-butylcarbaminoylcholine during the past one and a half years indicates that although this drug is less potent, it has some advantages over the tropine derivatives in routine internal examination of the eye and cycloplegic refraction. A combination of the new drug with one of the tropine derivatives may prove more effective than the use of either alone. The drug may also have advantages in the treatment of ocular inflammations; final evaluation will require considerable experimental work, as well as extensive clinical trial. Preliminary investigations indicate that the new drug has potent bactericidal properties and actions on the blood-aqueous barrier which are lacking with the tropine derivatives.

Di-n-butylcarbaminoylcholine sulfate is the most promising of the new choline-like derivatives to have an extensive clinical trial; however, the possibilities for development of more effective derivatives in this new field of pharmacology have not been exhausted. The most promising new compounds are surface-active, nitrogen-substituted carbamic acid esters of diethylaminoethanol. One of these compounds is the di-n-butylcarbamic acid ester of diethylaminoethanol hydrochloride. This compound has strong mydriatic and cycloplegic action but is more irritating than the corresponding quaternary ammonium derivative.

SUMMARY

We have recently synthesized a new class of choline esters with mydriatic and cycloplegic properties. Of the new drugs, di-n-butylcarbaminoylcholine sulfate most nearly meets the ideal requirements for use in cycloplegic refractions and routine internal examination of the eye. While less potent than homatropine in equal doses, the new drug has several advantages, notably, shorter action and negligible systemic effects from ocular administration.

State University of Iowa College of Medicine.

HEALING OF THE IRIS IN RABBITS FOLLOWING EXPERIMENTAL IRIDECTOMY

RUBY KATHRYN DANIEL, M.D.
DALLAS, TEXAS.

Surgical iridectomy has been used to advantage in treatment of a variety of conditions in the human eye. It has been employed rather widely in selected cases of glaucoma, in conjunction with removal of the cataractous lens and for the purpose of making artificial pupils. The prolonged or permanent gain from such a procedure has been explained by the assumption, based largely on clinical observation, that under its usual conditions the iris tissue does not show evidence of ability to regenerate, and, further, that under aseptic conditions the iris in its normal environment does not appear to produce connective tissue with which to form a scar or to fill in a surgically made defect in the iris.

Collins and Mayou [1] expressed the belief that aseptic wounds of the iris, such as are made in a surgical iridectomy showed no tendency to formation of scar tissue and that, except for the absorption of blood, the appearance of the iris wound remained precisely the same as when it was first made. They did not note any extension around the cut surfaces of the endothelium of the anterior surface or of the pigment epithelium of the posterior surface. Also, according to Parsons,[2] there is no formation of true scar tissue in the iris after a wound is made, although the gaping wound is usually filled with a blood clot, which later forms a granular mass in which fibers may be seen. It was also stated by Parsons that "uncomplicated wounds of the iris have had scant attention, and it is probable that important facts might be discovered by reinvestigation."

It was in an effort to find out the nature and type of healing which does take place after iridectomy that the surgical and laboratory procedures described in this paper were undertaken.

COMPARATIVE ANATOMY OF THE IRIS IN RABBIT AND IN MAN

The iris in the rabbit is rather similar to the iris in man in that it has a loose, cellular stroma containing vessels, nerves and unstriped muscle. Under normal conditions there is a small amount of fine fibrous tissue, which has branching spindle-shaped and star-shaped cells with elongated, interlocking processes. In the white rabbit, with blue irises, few or no pigment granules are seen in the sections stained with hematoxylin and eosin.

Briefly, the larger vessels in the iris run generally in a radial direction except for the circulus arteriosus iridis minor (called the circulus vasculosus iridis minor by Mann [3] because of its arteriovenous anastomosis), which lies not far from the pupillary edge. In the region of the ciliary body lies the circulus arteriosus iridis major. The arterial vessels of the iris belong to the ciliary system and are derived, in the rabbit, from the internal ophthalmic artery.[4]

The vortex and the ciliary veins [5] drain the venous blood from the iris, the ciliary body and the choroid. These veins empty into the orbital veins, which have three outlets: (1) backward, into the cavernous sinus and the intracranial system; (2) forward, through the facial system, and (3) downward, through the pterygoid plexus. While in man the return of venous blood of the orbit is largely into the intracranial system, in the lower mammals the return is more and more to the extracranial system.[2]

Near the pupillary margin the stroma of the iris carries, in its posterior portion, and sometimes in its middle part as well, a ring of unstriped muscle, the sphincter iridis. Endothelium covers the anterior surface of the iris, and a double layer of epithelium, the posterior surface, their union being at the pupillary margin.

This work was done at the Animal Experimental Institute of the Mayo Foundation, Rochester, Minn.

Submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Ophthalmology, November 1938.

1. Collins, E. T., and Mayou, M. S.: Pathology and Bacteriology of the Eye, Philadelphia, P. Blakiston's Son & Co., 1925, p. 383.

2. Parsons, J. H.: The Pathology of the Eye, New York, G. P. Putnam's Sons, 1904, vol. 1, pt. 1, p. 287.

3. Mann, I. C.: The Development of the Human Eye, London, Cambridge University Press, 1928, p. 225.

4. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1934, vol. 1, p. 188.

5. Duke-Elder,[4] p. 144.

According to Fuchs,[6] the iris may be divided for convenience into two regions: the pupillary zone, central to the circulus minor, and the ciliary zone, peripheral to it. The ciliary zone, in turn, can be divided into a smooth part and a folded part, with one to seven concentric furrows, which are present on dilatation of the pupil. The iris in situ varies considerably in shape, the form depending on its state of contraction; in the fixed state the appearance varies with the area examined and the angle at which the section is cut.

In the rabbit eye small, ciliary-like, radial processes frequently extend along the posterior surface of the iris from the region of the ciliary body for a distance 1 to 2 mm. inward from the root of the iris. Near the limbus these radial processes give an appearance of fairly long, finger-like projections, and sometimes there are connecting circular ridges, which in cross section show a lattice-like formation. With the hematoxylin-eosin stain these processes of the iris and their connecting ridges appear to be similar in type and structure to the ciliary processes.

The anterior surface of the iris in the rabbit is relatively regular and smooth and contains no appreciable wrinklings or furrows in the fixed state if the pupil was small when the tissue was fixed, while in the human eye the anterior surface contains multiple small crypts.

It was observed that the diameter of the floor of the iris in the rabbit eye is considerably larger in proportion to the other gross measurements of the globe than that in the human eye. A typical iris floor in the adult rabbit eye measured 12 mm. in the vertical and 13 mm. in the horizontal diameter, while the globe measured 15 mm. anteroposteriorly, 17.5 mm. horizontally and 16 mm. vertically in the fixed state. The average human iris measures approximately 11.6 mm. in the horizontal and 10.6 mm. in the vertical diameter, while the anteroposterior diameter of the human globe is 24.3 mm., its transverse diameter 23.6 mm. and its vertical diameter 23.3 mm.

HEALING IN THE IRIS

In the classified scientific literature only one reference to original work dealing with the healing processes in the iris was found. This study was made by Papagno,[7] who observed that linear injuries through the full thickness of the iris may heal. He expressed the belief that miotics materially aided the healing of radial injuries and that mydriatics assisted the process if the slit was parallel with the sphincter muscle.

The effects of temperature and of various drugs and endocrine substances on cultures of iris tissue in vitro have been studied rather extensively in recent years. Sanjô,[8] in 1932, determined the influence of morphine, narcotine, papaverine and thebaine on the growth in cultures in vitro of epithelial cells of the iris and described the histologic changes in these tissues produced by these drugs. Such studies seem to indicate that iris tissue in vitro is affected considerably by the physical and chemical qualities of its environment. I do not know what part the chemical composition of the aqueous plays with respect to the power of the injured iris to regenerate or grow in vivo.

SURGICAL AND LABORATORY PROCEDURES

In order to ascertain the nature and extent of the healing processes which take place in the iris after surgical iridectomy, an experiment was carried out in which the eyes of large mature white rabbits were used.

These rabbits appeared healthy and received an ample ordinary diet for caged rabbits, both before and during the experiment. Except for infections of the respiratory tract, "snuffles" and pneumonia, pregnancies and a fatal injury from fighting, the physical condition of the animals remained generally good. The most frequent complication was snuffles, which is not surprising, as the experiment was carried out during January, February and March of a severe Minnesota winter.

After being received for the experiment, each rabbit was examined with regard to its general condition and for ocular anomalies or peculiarities. Each animal received an external ocular and an ophthalmoscopic examination. If the rabbit was accepted for the experiment, a metal number tag was placed around the neck by means of a metal chain, which was bradded on for continuous wear until disposal after enucleation.

At the time of operation meticulous care was taken to prevent infection and to devise and use a standard uniform surgical technic which offered the minimum amount of trauma and irritation to the ocular tissues.

Incisions were made in the limbus with a keratome, and a small toothless iris forceps was used for grasping the iris. Intraocular irrigations were not employed because of their possible irritative effect. If during the operation the anterior chamber filled with blood, gentle, persistent stroking of the cornea was carried out in an effort to remove the blood or the blood clot. After the operation no instillation was made or dressing applied. (On rare occasions early in the study the lids were sutured together, but this measure did not prove of aid, for the animal was considerably annnoyed

6. Fuchs, E.: Textbook of Ophthalmology, translated by A. Duane, ed. 5, Philadelphia, J. B. Lippincott Company, 1917, p. 27.

7. Papagno, M.: Alcune ricerche sul processo di riparazione delle ferite iridee (studio sperimentale ed istologico), Rassegna ital. d'ottal. **3**:17-27 (Jan.-Feb.) 1934.

8. Sanjô, K.: Influence of Morphine, Narcotine, Papaverine and Thebaine on Growth of Epithelial Cells of the Iris in Cultures in Vitro and Histologic Changes in These Cells Produced by These Drugs, Folia pharmacol. japon. (Brev.) **14**:5-6 (March 20) 1932.

by the sutures and frequently scratched the region. Hence suturing of the lids was discontinued.)

Twice each week the rabbits which had been operated on were examined routinely with a focusing lens, a hand slit lamp and an ophthalmoscope and observations recorded.

Stated intervals were allowed to elapse between operation and enucleation. One globe was removed immediately after operation; 5 globes were removed at the end of a four day period, and the remainder, at regular weekly intervals of from one to eleven weeks inclusive.

Immediately after enucleation each globe was placed in a dilute solution of formaldehyde U. S. P. (1:10) and transferred in a separate bottle to the pathologic laboratory, where (after lateral calottes were cut) some of the globes were embedded in pyroxylin and others in paraffin.

The technic for embedding in pyroxylin was as follows: Each opened globe was passed in succession through a series of bottles containing 50, 70, 80 and 93 per cent alcohol, absolute alcohol and absolute alcohol and ether, and was allowed to stand in each for twenty-four hours. Then the specimen was placed in a thin (3 per cent) solution of pyroxylin and after forty-eight hours was transferred to a thicker (6 per cent) solution for two days. Later the specimen, embedded in the 6 per cent solution of pyroxylin, was placed under a bell jar in the presence of concentrated sulfuric acid until the pyroxylin appeared well "set." The sulfuric acid was removed and an open bottle of chloroform put in its place for twenty-four hours. After this the specimen was removed from the jar and placed in a dish containing equal parts of chloroform and cedar oil for forty-eight hours, being transferred later to clear cedar oil and allowed to remain forty-three hours or longer. The blocked specimen was then placed on the head of a Spencer rotary microtome, and sections were cut at a thickness of 8 or 10 microns.

With the globes embedded in paraffin a simpler routine was carried out. The specimen was placed in 95 per cent alcohol overnight and then transferred to acetone for six or eight hours. Next it was placed in toluene and paraffin, in equal parts, for one hour and then changed to fresh paraffin alone for two hours, before being embedded in the paraffin block.

The sections were stained with hematoxylin and eosin. The procedure was as follows: The sections were washed twice in 80 per cent alcohol and then with distilled water. A hematoxylin stain was then applied for five minutes, and the sections were washed in 1 per cent hydrochloric acid. After being washed in ordinary tap water, the sections were placed in a saturated solution of lithium carbonate and again washed with tap water. Eosin was applied for two minutes, and the sections were washed several times in 95 per cent alcohol. They were then placed in carboxylene and allowed to stand for four minutes before they were washed in xylene. They were then mounted with balsam and a cover slip applied.

GROSS OBSERVATIONS

During the period of observation there was no gross evidence of infection in any of the globes. In 4 eyes a thin, veil-like material seemed to bridge part or all of the surgical defect. In 1 of the eyes a suggestion of bridging appeared four days after operation. In 2 of the 4 globes gross bridging was apparent in seven days, and in 1, in fourteen days. In 2 of these globes small hemorrhages occurred immediately after operation, and in 2 a slight hemorrhage was noticeable for the first time on the fourth day after operation. These hemorrhages were all gradually absorbed. The 2 hemorrhages appearing at the time of operation had disappeared by the seventh day. One of the small hemorrhages noted on the fourth day had disappeared by the tenth day, and the other was not observed after the fourteenth day. Microscopic study revealed no evidence of the thin, veil-like bridging in these globes.

HISTOLOGIC OBSERVATIONS

Microscopic studies revealed mild rolling or retraction of the cut margins of the iris in a few of the globes, but on the whole the cut edges remained as they were immediately after operation. Four days after operation the iris was extremely edematous and in many sections measured as much as three times its normal thickness. On the seventh day the edema was less pronounced, and on the fourteenth day the amount was slight. Except in 1 globe, all edema of the iris had disappeared by the twenty-first day. Hemorrhages, also, were not noted microscopically in any of the sections after the twenty-first day.

A study of sections from various areas and levels of the surgical defect in 5 globes removed four days after iridectomy revealed in 3 an early, feeble effort to bridge the defect with tissue. In these sections a blood clot filled the defect partially or completely, on the surface of which there extended a few to a continuous layer of cells resembling epithelium or endothelium, while the loose meshes of the blood clot appeared to support a few scattered spindle-shaped cells.

An iridectomy wound seven days old showed an extension of connective tissue from the cut surface of the cornea into the injured processes of the iris which were in close contact with the wound. Also, extending from the wound was a small ridge of dense connective tissue, running along in close proximity to, and even adjacent to, the inner surface of the intact Descemet membrane for a distance of 0.75 mm. The corneoscleral wound appeared to be well healed with connective tissue. The iris showed moderate hyperemia and edema.

Sections from both globes on which iridectomy had been done fourteen days previously revealed mild hyperemia and edema of the iris, as well as extensions of corneal connective tissue into the iris stumps. One area showed a small bridge of connective tissue which appeared to reach down

and cover the peripheral notch of the surgical defect in the iris and was attached, farther inward, to the cut surface of the iris. In the other globe, on which two iridectomies had been performed, a band of connective tissue bridged the limbic arc from one corneal scar to the other. In the fixed state this band was in close proximity to the anterior capsule of the lens. At one point the band was divided, and a strand extended behind the lens, in close proximity to the posterior capsule. From a study of various levels it could be determined that this connective tissue came entirely from the corneal scar and extended inward through the surgical defect in Descemet's membrane. In one of the areas of the iridectomy, a thin single layer of epithelium lay on an old, partially absorbed blood clot. This bridge was very fragile and short. The healing process here was no more advanced than that observed four days after iridectomy. In this globe, in which considerable postoperative reaction was grossly apparent, there was also a greater proliferation of corneal fibrous tissue inward than in the other globes, and the remaining iris appeared slightly more edematous.

After these sections of the fourteen day old iridectomy wounds, no sections of the surgical defect taken at a later stage showed even traces of cells springing from the iris. (I was unable to determine whether, after the first feeble attempt of the iris at repair, the failure of the process to progress was due to an inhibiting influence of the aqueous or to lack of viability of cells springing from the iris or to some other, unknown factor.)

All the sections did continue to show the ability of corneal fibroblasts to pass through defects in Descemet's membrane into the cut or injured surfaces of the iris and its processes, as well as occasionally to send an independent extension as a small ridge or, as in the case of the globe with considerable postoperative reaction (which may have been a mild inflammatory response), as an actual band or strand.

In the globe enucleated twenty-eight days after iridectomy, the defect in the iris was mechanically plugged near the limbus by normal, healthy-appearing processes of the iris. These processes did not have damaged surfaces and, although lying directly against the cut margins of the iris, did not show any signs of becoming adherent to or of fusing with the cut edges. The iris in the region appeared normal, and no edema was present.

In a globe enucleated thirty-five days after iridectomy a stump of the iris exhibited rounded free margins and dense infiltration with connective tissue cells, clearly arising from the corneal scar at the limbus. In the second globe, removed thirty-five days after operation, in addition to the iridectomy, the lens had been removed by extracapsular extraction, and the capsule remained as a folded mass (resembling a ribbon in the section) in a part of the wound. The capsule appeared slightly swollen but otherwise intact, and fibroblasts had been unable to penetrate it. Hence the otherwise firmly healed wound had a defect corresponding to the capsular material, but a thin band of fibrous tissue had formed around the outer margin. The sections containing defects in the iris in eyes enucleated forty-two, forty-nine and sixty-three days after iridectomy showed no further healing. The iris in these sections was free from edema and hyperemia.

One of the globes removed seventy-eight days after iridectomy showed remnants of iris tissue embedded in the corneal scar. The iris retained its structural characteristics and was easily recognized, but was permeated with connective tissue cells, apparently springing from the corneal stroma.

The accompanying photomicrographs illustrate the appearance of the iris before and at several stages after iridectomy.

The normal control section (fig. 1) was taken from the region of the angle of the anterior chamber. The gross appearance of the globe was normal. The cornea was normal; the anterior chamber was filled with normal-appearing aqueous; the pupil reacted to light, and the iris, which was blue, showed no abnormality. Microscopic study of cross sections of the specimen revealed the stratified pavement epithelium of the cornea merging at the limbus with the epithelium of the conjunctiva. The vascularity (superficial marginal vessel loops) of the superficial layers of the cornea was seen in the region of the limbus. The corneal stroma was in orderly layers. The structureless Descemet membrane could readily be made out, as well as the single layer of endothelial cells, which on cross section appeared rectangular, with a slightly oval nucleus and abundant protoplasm.

The meshwork at the angle of the iris had been slightly disturbed on section but filled part of the depression of the scleral furrow. The tissue of the iris was normal in appearance. It was made up of a loose meshwork of stroma containing vessels, nerves and unstriped muscle. Its anterior layer of endothelium and its posterior surface, composed of a double layer of epithelial cells, were intact. A ciliary process extended

from the posterior region just opposite the angle of the root of the iris (fig. 1).

The eyes which presented the most significant early changes were those enucleated four days after iridectomy. Of these 5 globes, 3 showed small gross hemorrhages at the time of removal. Microscopic study of these 3 globes also showed appeared to do so with some degree of regularity, and the spindle-shaped cells within the body of the clot were extremely sparse and did not give definite evidence of their origin (fig. 2).

Forty-two days after operation the appearance of the region of the iridectomy wound had changed considerably. A dense old fibrous con-

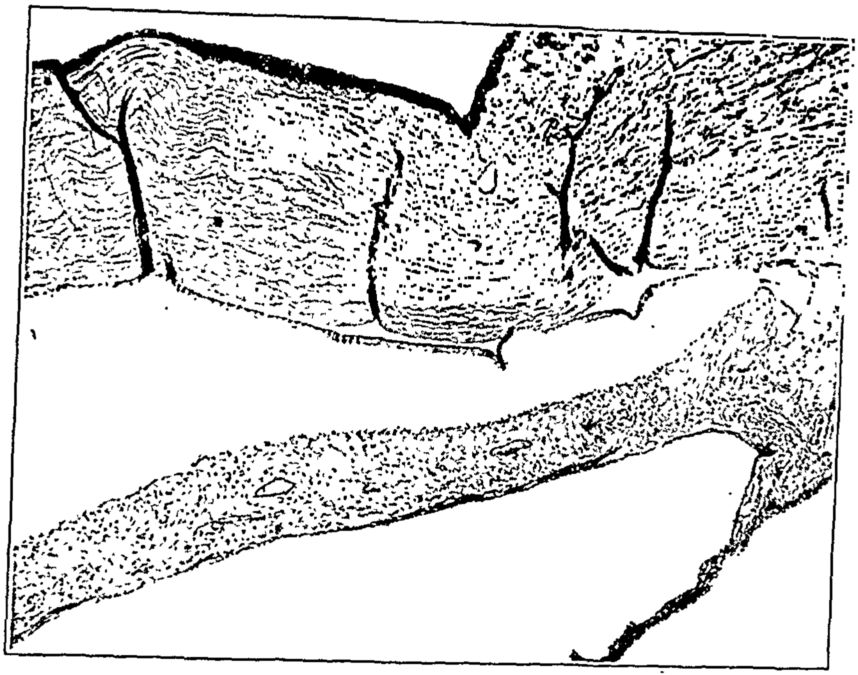

Fig. 1.—Normal cornea and iris in the rabbit (× 40).

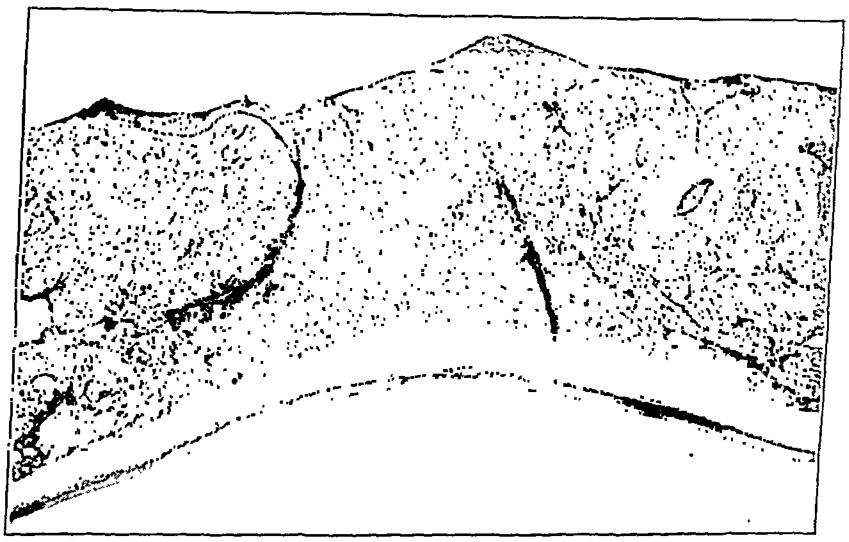

Fig. 2.—Iridectomy four days after operation, showing edema of the iris and proliferation of endothelial cells into the blood clot filling the defect in the iris (× 40).

blood clots in the area of the iridectomy. The anterior chamber was filled in all the eyes, and neither gross nor microscopic inspection revealed any leakage of the wound. Microscopic sections of these 3 globes showed an early attempt at organization of the blood clot in the surgical wound. There was considerable edema in the iris tissue in each globe. The endothelial cells which extended out on the surface of the clot nective tissue scar, which had produced considerable indentation in the cornea, lay just beneath the conjunctival margin. The vascularity of the limbic region (superficial marginal vessel loops) was plain, and the proliferation of the connective tissue at the corneoscleral junction in a somewhat irregular fashion or layering was evident. A wide break occurred in Descemet's membrane, with each end curling slightly upward.

Proliferation of connective tissue appeared to fill in the gap between the two ends of this membrane. Below this gap, also, tissue and processes of the iris were adherent to the inner surface of the scarred cornea. There was no evidence of regeneration of the iris or of origin of fibrous connective tissue in the iris itself. Some processes of the iris and remnants of such healing process. Here, again, there was no proliferation of fibrous tissue in the remnants of iris in the region of the corneal incision and the peripheral iridectomy wound. Some iris tissue was included in the wound, and the stroma had maintained its characteristics and had not formed dense fibrous connective tissue within itself, although it lay close to the fibrous tissue arising

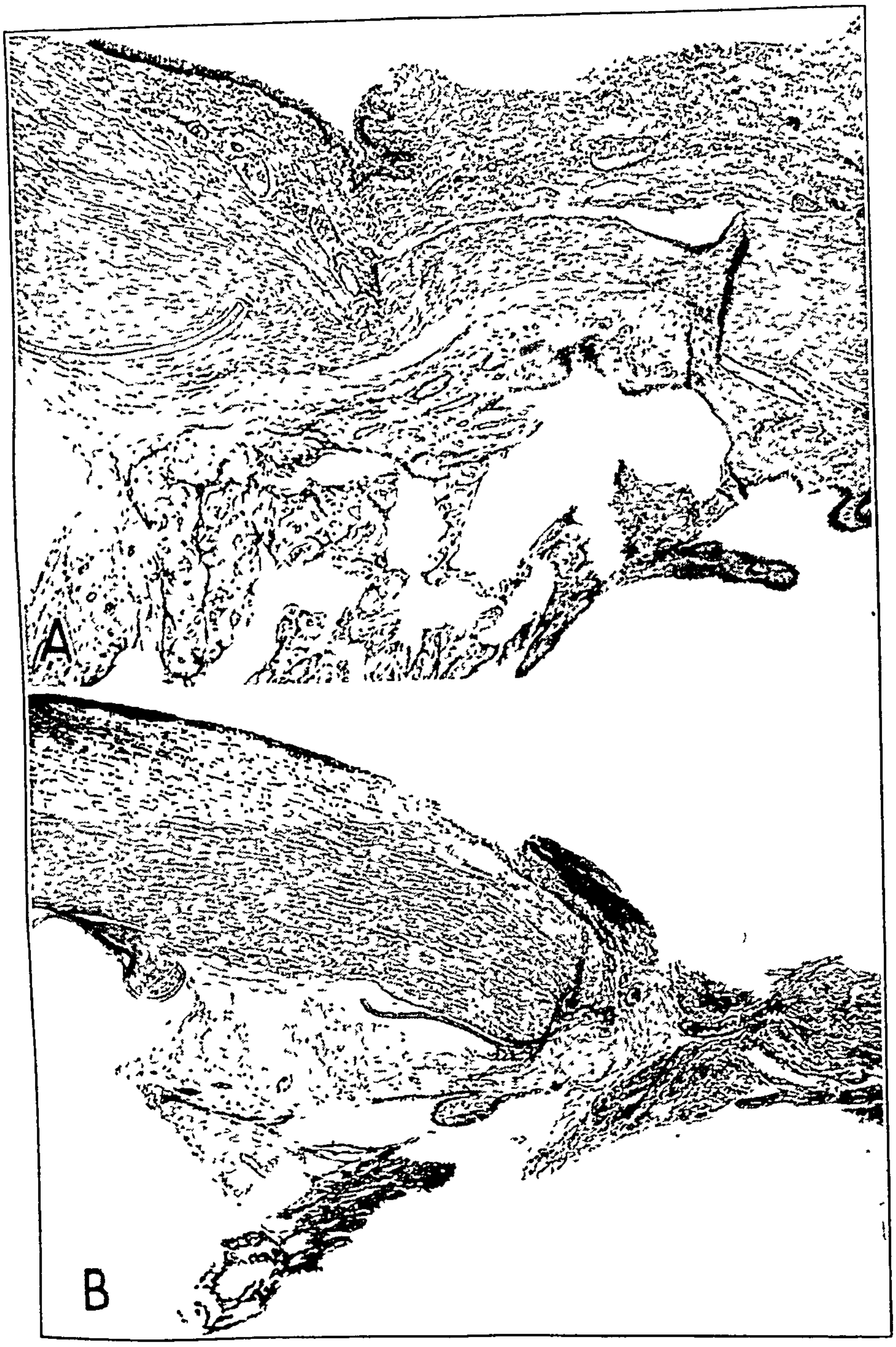

Fig. 3.—*A*, area of incision in the cornea, with the iris adherent to the cornea forty-two days after operation. *B*, corneal scar and fragments of iris in the region of iridectomy at the corneoscleral junction seventy-eight days after operation (× 40).

processes were present below the adherent stroma of the iris. No evidence of hemorrhage was seen. A few lymphocytes were scattered in the scarred region, particularly near its surface (fig. 3 *A*).

Sections of the eyes seventy-eight days after iridectomy showed no striking change in the from the cornea and the sclera. The ciliary processes included in the area of the wound were hyperemic and distorted. Near the left central part of the section was a break in Descemet's membrane, with its characteristic outward curl of the ends. There was no evidence of regeneration of the membrane between these two ends.

SUMMARY

In this study the following observations were made:

(1) Failure of iris tissue to regenerate itself after surgical iridectomy. (2) Failure of the iris of itself to bridge the surgical coloboma with permanent fibrous scar tissue, even though four days after operation 3 globes showed an early, feeble attempt to bridge the defect with a few scattered fibroblasts and a surface layer of epithelial or endothelial cells. Later no permanent bridging with tissue arising from the iris was observed. The tissue and the cut surfaces of the iris remained unchanged. (3) Frequent and prolific invasion of corneal fibroblasts into the approximated cut edges of the iris in the region of the wound. (Descemet's membrane appeared to function somewhat as a barrier. When it was perforated and the corneal stroma was cut in that region, the fibroblasts originating from the cornea could rapidly invade the damaged tissue or stump of the iris in that area.) This could, and did, occur in a moderate degree even when healing of the (incision) wound was rapid and firm, when the iris was not caught in the wound itself, and when there was no gross or microscopic evidence of infection or inflammation.

Medical Arts' Building.

PARALYSIS OF DIVERGENCE DUE TO CEREBELLAR TUMOR

OTTO LIPPMANN, M.D.
AUSTIN, TEXAS

There is no generally accepted opinion as to the mechanism of divergence in human eyes. Some authors (Duke-Elder,[1] Pugh, Alfred Graefe and others) have assumed that divergence is merely a passive function resulting from relaxation of convergence. Brouwer's theory of a convergence center located in Perlia's nucleus has almost universally been accepted (Riley [2]). The majority of observers find it difficult to believe that of all well regulated functions divergence alone should be without a definite innervation. If the limit of divergence were identical with a position of rest due to complete relaxation of convergence, every person who loses the ability of fusion ought to manifest divergent strabismus, whereas only a certain percentage do. Bielschowsky [3] stated that active divergence innervation is necessary to overcome esophoria. On the basis of neuromuscular physiologic observations, Bruce [4] stated that his conception of ocular divergence was that of a combined passive (i. e., elasticity of the external rectus muscles) and active function.

Knowledge of the centers and paths for divergence is even more scant. Although the proponents of active divergence function assume the existence of such a center, Bruce admitted "that reasoning will have to be guided by deduction rather than influenced by definite proof." He concluded that Hering's "faculty of attention" indicates the presence of a higher, cortical center. "The avenues connecting these higher centers with the lower ones are not well known." [4] It may be deduced that the "cerebral centers as well as the descending paths must be bilateral.[4]" It is conceivable that lesions in the cortical centers and in the descending bilateral paths cause paralysis of divergence, but other symptoms are likely to predominate. Pure divergence paralysis is likely to be caused by a lesion in a lower, subcortical center for divergence. There are on record cases of pure divergence paralysis in which true paralysis of the abducens nerve later developed. Bielschowsky, Bruce and others therefore postulated "the existence of a center for divergence separate from, but adjacent to, the nucleus of the sixth cranial nerve. Since the external rectus muscles are innervated only ipsilaterally, this nucleus would probably be in the midline."

Haessler,[5] in a recent review of this subject, differentiated between divergence as a "well established functional unit" and the "act of diverging." He expressed the opinion that divergence is possible as a "result of an orderly sequence of impulses to the individual muscles, just as fingers are moved . . . in such complex acts as playing a musical instrument." Divergence, accordingly, would not require a real center of preformed anatomic masses. Divergence would habitually be carried by the same neurons as a conditioned reflex. But Haessler expressed the opinion that the anatomic location of these neurons would also be in the brain stem. He admitted that the differentiation between an embryonically preformed center and these undifferentiated neurons is an academic question.

I shall not deal with the diagnosis or the differential diagnosis of divergence paralysis, since this paper is concerned with the evidence of a center for divergence. However, I shall list briefly the causes of divergence paralysis which have been mentioned in the literature (Prangen and Koch,[6] Davis [7] and others). In most cases of weak divergence insufficiency the disorder is functional. The more pronounced paralyses of divergence have been due to a variety of organic diseases of the brain: encephalitis, syphilis, diphtheria, poliomyelitis, chorea, tabes, lead poisoning, hemorrhage, vascular diseases of the brain stem, migraine, multiple sclerosis and cerebral tumor.

1. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1933, vol. 1.
2. Riley, H. A.: The Central Nervous System Control of the Ocular Movements and the Disturbances of This Mechanism, Arch. Ophth. **4**:640 (Nov.); 885 (Dec.) 1930.
3. Bielschowsky, A.: Lectures on Motor Anomalies of Eyes: Paralyses of Conjugate Movements of Eyes, Arch. Ophth. **13**:569 (April) 1935.
4. Bruce, G. M.: Ocular Divergence: Its Physiology and Pathology, Arch. Ophth. **13**:639 (April) 1935.
5. Haessler, F. H.: The Divergence Impulse, Arch. Ophth. **26**:293 (Aug.) 1941.
6. Prangen, A. DeH., and Koch, F. L. P.: Divergence Insufficiency: A Clinical Study, Tr. Am. Ophth. Soc. **35**:136, 1937.
7. Davis, W. T.: Diagnosis and Treatment of Phorias, Am. J. Ophth. **21**:145, 1938.

Although the existence of a center for divergence has found so many proponents, authentic pathoanatomic evidence of such a center is almost entirely lacking. I have found only 1 case reported with autopsy, that of Bender and Savitsky.[8] In their case paralysis of divergence was the first and only symptom during most of the clinical course, and autopsy revealed a small hemangioma in the central gray matter and the periaqueductal area at the level between the superior and the inferior colliculi. They expressed the opinion that a center for divergence exists in this area. The same authors cited another case (reported by Straub) of paralysis of divergence associated with a tumor in the middle fossa; no other details were given. Holden[9] mentioned briefly, without other information, a case of paralysis of divergence associated with a tumor of the midbrain. Howard[10] reported a case associated with roentgenographic evidence of multiple metastases of carcinoma of the breast to the cranial bones and the sella turcica. Destruction of the center for divergence by a metastatic tumor of the brain was assumed, but no report of autopsy, follow-up observation or further information was furnished.

The report of a case of paralysis of divergence, the clinical observations in which were confirmed by direct inspection during operative exposure is likely to increase knowledge concerning the center for divergence. The patient, whose chief symptoms were headache and paralysis of divergence during most of the clinical course, was under my observation for more than two years.

REPORT OF A CASE

H. N., a college student aged 20, first consulted me on Dec. 4, 1939. His chief complaints were daily bilateral headaches, mostly localized in the occipital area, usually lasting only an hour at a time and first appearing several months before; dizziness when he stooped, and a slight nasal discharge.

Past History.—There was a history of (1) occasional vomiting in the morning, which had previously been diagnosed as a symptom of gastric ulcer; (2) slight nasal obstruction in childhood, diagnosed as an allergic condition, and several attacks of asthma, and (3) injury to the head through a fall from a horse one year prior to the appearance of headache. This accident resulted in concussion of the brain, but there was no fracture of the skull. Six weeks after the accident the attending physician made the diagnosis of constriction of the visual fields, a condition which disappeared in about ten weeks. (4) The patient had worn glasses for several years.

Examination of the Eyes.—The lids, the anterior segment, the media and the fundus of both eyes were normal. The pupils reacted normally to light and in accommodation. Pronounced nystagmus in the extreme lateral direction of gaze could be observed. The movements of both eyeballs were normal. Tests for heterophoria revealed 5 prism diopters of esophoria for distance; 1 prism diopter of hyperphoria in the right eye, and almost complete orthophoria at reading distance. Tests for vergence revealed 2 prism diopters of positive vertical divergence, 2 prism diopters of negative vertical divergence, 1 prism diopter of abduction and 8 prism diopters of adduction.

With a correction of —0.25 D. sph.—0.75 D. cyl., axis 90 for each eye, vision was 20/20—1 in the right eye and 20/20 in the left eye.

Otorhinoscopic Examination.—The ears were normal. Inspection of the nose showed hypertrophy of all the turbinates, with pale mucous membranes.

Diagnosis and Subsequent Course.—Divergence insufficiency was suspected, and further observation was planned. A diagnosis of mild vasomotor rhinitis was also made.

Owing to the patient's attendance at a college in another town, he was not seen until May 1940. At that time he stated that his nasal symptoms had improved and that the headaches, dizziness and vomiting had disappeared. He now complained of diplopia in all directions of gaze except when he looked straight upward.

Tests for diplopia with the red glass confirmed his statements. There was esotropia of 6 prism diopters, with no change in the angle of squint in lateroversion and infraversion. The convergent deviation disappeared on supraversion. There was no diplopia on his looking straight upward. When he looked to the left and upward the right eye was higher, and when he looked to the right and upward the left eye was higher. The primary and the secondary angles of squint were equal. The horizontal amplitude of fusion was approximately the same as it was in December 1939 (8 prism diopters). The near point of accommodation was 11 cm. The nystagmus was the same as in December 1939. The impression was that of a possible spasm of both inferior oblique muscles. Since the question of spasm of individual ocular muscles is problematic, no definite diagnosis was made. The vertical deviation was not found again in subsequent examinations during the following years.

On June 13, 1940 caloric tests of both labyrinths showed hypersensitivity on stimulation of either side, the left side being slightly more sensitive than the right. The refractive error and the amount of horizontal deviation were the same as in December 1939 (the vertical deviation had disappeared). Prisms base out were prescribed for distance, a correction of —0.75 cyl., axis 90 ⊃ 3 Δ base out being worn in each eye. A few days later the patient reported that he was comfortable and had no diplopia when he wore the new glasses.

In August 1940 diplopia appeared again, in spite of his wearing the glasses; the esophoria for distance had increased to 12 prism diopters. The diagnosis of typical paralysis of divergence was now definite.

In September 1940 the paralysis of divergence was unchanged (with no diplopia at reading distance). When a fixated object was slowly moved away from the eye, diplopia appeared at a distance of 1 meter. Tests of fusional amplitude showed further decrease of abductive power but improvement in adduction. Exercises with prisms failed to produce any improvement.

In June 1941 the esophoria for distance had increased to 15 prism diopters. The patient complained of constant headache, constant diplopia and beginning signs of mental involvement ("lack of interest"). Vision, the

8. Bender, M. B., and Savitsky, N.: Paralysis of Divergence, Arch. Ophth. **23**:*1046* (May) *1940*.

9. Holden, W. A.: The Ocular Manifestations of Epidemic Encephalitis, Arch. Ophth. **50**:101, 1921.

10. Howard, C. P.: Divergence Paralysis, Am. J. Ophth. **14**:*736*, 1931.

results of refraction and the appearance of the fundi were unchanged. The impression at this time was that of an organic lesion of the central nervous system, and neurologic consultation was advised. The patient did not submit to a complete neurologic examination until January 1942, when he was admitted to John Sealy Hospital of the University of Texas Medical School, Galveston, Texas. Dr. S. R. Snodgrass permitted me to use the hospital records, data from which are submitted.

Hospitalization.—The patient was admitted on Jan. 31, 1942 and discharged on Feb. 21, 1942, with the diagnosis of intracranial tumor. He was admitted a second time on March 1, 1942 and died on March 14, after suboccipital exploration. The diagnosis was cerebellar tumor.

Ophthalmologic Consultation (January 31): The visual fields were normal. There was blurring of the margins of the disks, but no definite elevation. Nystagmus was noted in all directions of gaze.

Neurologic Examination (February 6): Examination revealed ataxia to the right side and to the left, the disturbance being more pronounced on the left side; dyssynergia of the arms (worse on the left side than on the right); increase in the deep reflexes; motor weakness of the left lower part of the face and the left arm, and absence of sensory changes.

Laboratory Data: Laboratory examinations revealed nothing abnormal. The roentgenogram showed enlargement of the sella turcica and thinning of the posterior clinoid processes. There was no evidence of an old fracture. No definite etiologic diagnosis could be made, but exaggeration of the digital markings indicated increased intracranial pressure. The lesion was thought to be intramedullary or cerebellar. (A cerebral location was also considered.)

The patient left the hospital unimproved. On the second admission, the predominant symptoms were headaches, stiffness of the neck and staggering gait.

Operative Record (March 12).—Dr. Snodgrass made a suboccipital exploration, with partial removal of a cerebellar tumor. Great difficulty was encountered during the first part of the anesthesia, the respiratory rate falling to 4 per minute; operation could be started only after one hour, during which complications were combated. The usual cerebellar incision was made; ventricular pressure was observed to be increased, and clear spinal fluid was withdrawn through a needle until the pressure was normal. The bone over each cerebellar hemisphere was widely removed. The dura was opened first over one hemisphere, then over the other and then laterally across the midline, after division of the occipital sinus between silk sutures. A large tumor, apparently arising in the vermis, filled the cisterna magna almost completely and extended downward. "This tumor was smooth, pinkish brown and firm." A portion of the atlas was then removed and the dura opened down to the second cervical lamina. "The same tumor extended downward to a point completely out of sight. It entirely hid the posterior surface of the cord, as well as the medulla." Frozen sections made during operation were reported as revealing astrocytoma. The lower part of the tumor, measuring 1.5 by 1.5 cm., was withdrawn from the spinal canal without particular difficulty. Slight adhesions to the medulla were noted. The upper end of the tumor (main part) was bluntly dissected from the cerebellum. "It appeared definitely to originate in the vermis." Additional large portions of the central solid portion were then removed by sharp dissection. Obstruction of flow of the cerebrospinal fluid from the ventricles was apparently relieved by the operation. Irregularity in the pulse and adhesions to the medulla made complete removal of the tumor inadvisable. The wound was closed, and transfusions and infusions of dextrose were given.

Pathologic Report (Dr. Paul Brindley; March 20, 1942).—The specimen consisted of seven pieces of tissue, the largest measuring 8 by 6 by 5 mm. and the smallest 2 by 1 mm.

Microscopic Examination: A moderate amount of hemorrhage was noted in a few sections and a rather notable increase of vascularity in all. The blood vessels were all congested. The number of cells was increased in many places, these cells being small, round and dark staining, while in other places the cells were larger and had a somewhat vesicular nucleus. Glial tissue was increased throughout the sections, particularly in the areas where the cells were large and had vesicular nuclei. Some sections showed many small oval calcified bodies. The cells were not pleomorphic. They were all of the one or two types described. In a few places the large cells had a whorl-like arrangement, but this was not uniform. Stains for reticulum and the trichrome stains did not define the nature of the growth any more clearly.

Diagnosis.—The appearance of this tumor was not typical of medulloblastoma, ependymoma or hemangioblastoma, which, with astrocytoma, constitute the cerebellar tumors. Owing to the endothelial proliferation of blood vessels and the conspicuous vascularity, it was impossible to call the tumor an astrocytoma. Special stains did not aid in a more definite diagnosis.

Outcome.—The patient did not respond well to the serious operative procedure and died without regaining much cortical faculty.

COMMENT

Knowledge of the mechanism and the subcortical center for divergence of the eyes in man is incomplete. A review of the literature reveals that the majority of authors have assumed the existence of a center for divergence which is probably located in the metencephalon, in the vicinity of the nucleus of the abducens nerve. Pathoanatomic proof is almost entirely lacking. Only 1 case of paralysis of divergence with autopsy was found; in this instance the authors claimed a center for divergence in the mesencephalon (not far from the nucleus of the oculomotor nerve).

In the case described here paralysis of divergence was the chief symptom during most of the clinical course. Direct inspection during operative exposure proved that the lesion in this case was a tumor of the vermis, extending downward along the medulla. Pressure from the tumor impeded the flow of the cerebrospinal fluid. It is most likely that pressure by the tumor on the subcortical center for divergence caused the paralysis of divergence. A tumor of the vermis of the cerebellum could exert pressure only on the metencephalon. This case, therefore, supports the theory of a center for divergence in the vicinity of the nucleus of the sixth cranial nerve.

FURTHER EXPERIENCES WITH A SYSTEM OF INTRACAPSULAR EXTRACTION OF CATARACT

DANIEL B. KIRBY, M.D.
NEW YORK

The development of a system in any endeavor is worth while. It means an orderly marshaling of one's thoughts and ideas on the subject in hand. This is particularly applicable to the matter of cataract extraction because of the many variables, contingencies and complications which may arise. The surgeon may well review these various situations and his methods of meeting them. I was trained in extracapsular cataract surgery and practiced it for ten years. Now I have had an equal period of experience with the intracapsular method, having adopted it after achieving satisfactory results in selected cases. I have published an article dealing with original variations from published technics and incorporating a new method to be used in coping with difficulties. I became aware that the descriptions of intracapsular technics in the literature did not take into account the observations which should be made before and after each manipulation of the operation and what should be done in case the particular maneuver advocated did not succeed in accomplishing its intended purpose or a complication arose during the maneuver. I have assembled a series of technics, some from the experience of various surgeons, as recorded in the literature, and others which I have devised myself, and have arranged them in a system in which my desire is to fit the maneuver to conditions present and to situations as they arise in the course of the operation. To make the system complete, I have also given attention to the matter of subluxated and luxated lenses. In this paper I shall review briefly the technics as applied to cataracts with intact zonules and the results in 100 consecutive cases occurring within the past two and one-half years in which the intracapsular technic was applied.

The literature has previously been reviewed and contributions, particularly those of Knapp and Verhoeff, acknowledged. The indications for operation, and examination of the patient, the sedation, the induction of anesthesia and akinesia and the postoperative management have beeen described elsewhere.

Read at the Seventy-Ninth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 10, 1943.

THE CAPSULE AND ZONULE

The principal variables for consideration are the conditions of the capsule and the zonule of the lens. Undoubtedly there exists as a cause or as an accompaniment of the development of cataract a degree of degeneration of the capsule and of the zonule. I have never attempted the removal of the normal living, healthy human lens, but I have plans for testing the resistance of the capsule and zonule in eyes from which the normal anterior segment has been removed, for example, because of melanosarcoma. I tested these features in the eyes of a healthy 10 year old monkey and found resistance and resilience much greater than I have ever encountered in the human lens with cataract.

Types of Zonules.—The zonules in cases of cataract may be classified roughly into three types: (1) fragile zonules, which rupture easily, permitting removal of the cataract by traction or pressure alone, approximately 15 per cent; (2) zonules with average resistance, which require pressure plus traction and rotation, both clockwise and counterclockwise, for delivery, 70 per cent, and (3) zonules with more than average resistance,. extraction being accomplished by pressure, traction and rotation and, in addition, stripping of the zonule from the upper third of the equator of the lens, 15 per cent.

It will be well again to describe briefly the three efforts and certain other details of the procedure as applied to the various types of cataract, so that the results may be better understood.

OPERATIVE PROCEDURE

Incision and Appositional Sutures Inserted After Incision.—The incision is made in the limbus for one-third the length of the circumference, and it may be enlarged to one-half or two-fifths. It is purposely placed slightly forward to avoid the bleeding encountered with a deeper incision. If the conjunctival flap is wider than 1 mm., the incisions are made radial to the edge of the cornea at 10:30, at 12 and 1:30 o'clock, to permit the better placement of the appositional sutures at these points in the dense corneoscleral tissue. The central suture is used

to retract or to elevate the corneal flap in order that a direct, clear view of the iris and the capsule of the lens may be afforded during the iridectomy and the application of the forceps to the lens capsule. This maneuver is conservative and facilitates operation. It permits of manipulations not otherwise possible. It does not appear in itself to lead to any complications, such as striped keratitis, bullous keratitis, corneal opacity or loss of vitreous, as judged by the experience and the results obtained during the past six years. It is of aid in preventing injury of the endothelium by instruments. One may lift the flap after the delivery of the cataract to view the position of the iris. If the iris is not incarcerated, the use of the iris repositor is avoided. The lifting of the corneal flap can be definitely recommended.

Handling of the Iris.—Retention of the round pupil with peripheral iridotomy is desirable and may be attempted if the pupil will dilate to 6 mm. or more. If it will dilate to 5 mm., retention should be attempted only for small cataracts. If the iris will dilate only to 4 mm., complete iridectomy is necessary. Complete iridectomy is desirable in difficult cases or in cases in which a proper grasp of the peripheral part of the capsule, near the equatorial region, is not feasible. The iris may be retracted with the forceps or with a blunt, flat hook to expose the periphery. A miotic is used after the successful intracapsular operation, even when a complete iridectomy has been performed.

The Three Efforts as Applied to the Three Classes of Zonules.—Effort 1: Preliminary Pressure: Pressure is exerted with the flattened point of the lens expression hook. The points of application of pressure are inside the corneal ring, or limbus, at 4, 6 and 8 o'clock on the corneal dial. Application of pressure may be repeated once or twice. The degree of pressure is such that the cornea is indented 2 or 3 mm. A contraindication to exertion of pressure on the cornea is increased intravitreous pressure. One effect of the pressure may be subluxation of the lens through rupture of the lower portion of the zonule in cases of cataract with a fragile zonule, resulting in relaxation of the capsule. If subluxation does not occur, the maneuver has not been useless, for the surgeon has been able to make observations on the resistance of the eye and the size and consistency of the cataract and to prepare himself for the manipulations necessary for removal of the particular cataract. After the preliminary pressure, if the cataract is subluxated below and is "tumbling," it may be removed by pressure alone. If the lens is subluxated and shows no tendency to "tumble," traction may be applied for delivery. If the lens is not subluxated, it may be delivered by traction, pressure and rotation (effort 2) or, finally, by stripping of the resistant zonule (effort 3).

Effort 2: Traction, Pressure and Rotation: Traction, pressure and rotation, both clockwise and counterclockwise, are applicable to cases of cataract with zonules of average resistance. The forceps are applied above to the anterior face of the equatorial region. 1. Traction is exerted at 12 o'clock and pressure applied directly opposite, at 6 o'clock. 2. The forceps are rotated clockwise at 2 o'clock and then held still, while pressure is applied directly opposite, at 8 o'clock. 3. The forceps are rotated counterclockwise to 10 o'clock and then held still, while pressure is made directly opposite, at 4 o'clock. Indications of rupture of the zonule are watched for. The entire process may be repeated once, and possibly a second time. When subluxation has occurred, complete luxation and delivery may be effected by use of various parts of these manipulations, according to indications. The final extraction is made by sliding or wheeling out the cataract.

Effort 3: Stripping of the Zonule: This procedure is resorted to in cases of an elastic, resistant zonule, recognized as a membrane reenforced by fibers. The capsule must be grasped at or near the upper equator of the lens in order to tilt and lift the latter 3 mm. above the hyaloid membrane. The hyaloid membrane normally does not appear to adhere to the posterior capsule. Before the surgeon resorts to stripping off the zonule, the manipulations of traction, pressure and rotation must be given a full trial, within the limits of safety. A recent, and the only, experience with loss of vitreous in relation to stripping of the zonule was enough to impress this. It is necessary before one strips the zonule to make sure that the capsule is grasped above and near the equator, so that the lens may be tilted and the edge lifted away from the hyaloid membrane. Stripping of the zonule is accomplished by three steps: 1. Touching of the zonular membrane, which has been made tense by traction of the forceps on the capsule at 12 o'clock on the corneal dial. A dehiscence or hole in the zonular membrane may be seen to form. 2. Rotation of the forceps and lens clockwise to 2 o'clock, with stripping between 12 and 10 o'clock. 3. Rotation of the forceps and lens counterclockwise to 10 o'clock, with stripping between 12 and 2 o'clock. Tearing of the zonule and enlargement of the opening may be observed when the lens is rotated clockwise and counterclockwise. Further tearing occurs on rotation with pressure applied directly opposite the point

of traction. After the area of the zonule between 10 and 2 o'clock, representing 120 degrees, has been stripped, complete luxation and delivery are accomplished by traction, pressure and rotation, the lens finally being slid or wheeled out.

Combinations of Maneuvers.—These maneuvers are not described for the purpose of establishing any of them as effective in cases of all kinds. They are of value only when combined in a system which may be varied to suit the individual situation as it arises in the particular case.

Reason for Exertion of Pressure Opposite the Point of Traction.—Observations on the behavior of the capsule under traction show the creation of a principal fold about 2 mm. wide, running from the point of traction to a point in the zonule directly opposite. Pressure is exerted at a point just inside the ring of the limbus of the cornea, where the zonule joins the capsule, in case the former is intact. It stands to reason that pressure over the fold of zonule which is tense will be more effective in rupturing it if applied at a point (approximately the 2 mm. area of the lens expressor hook) rather than over a larger surface. It is also reasonable that the pressure should be applied to the tense fold, and not to the relaxed area of the zonule on either side of the fold, and such pressure is certainly much more effective than any applied outside the ring of the corneal limbus. The same reasons apply to stripping of the zonule in the area made tense by traction in the opposite direction.

Nonrepetition of an Ineffective Maneuver.—The rationale of a system of intracapsular cataract extraction is the development of a series of observations, opinions and maneuvers by which the surgeon has some maneuver in reserve in case the procedure which he had planned or employed fails of its object. It need not be said, however, that he will routinely use any one procedure or apply it unless it carries a reasonable expectancy of success. A maneuver which has been applied once and has failed to accomplish its purpose is not repeated.

RESULTS AND OBSERVATIONS

After this brief description of the methods as they are applied in cases of cataract with intact zonules, a series of cases in which the various maneuvers were employed as indicated may be reviewed with profit. No case was omitted because it was complicated or because the capsule ruptured. One hundred consecutive cases occurring since my original paper was prepared, in 1941, in which the attempt was made to remove the lens in capsule are analyzed.

Capsule.—In 90 cases the cataract was removed in capsule without rupture. In 1 case the capsule ruptured, but the capsule was removed in its entirety after delivery of the nucleus. In 9 cases the capsule ruptured and the operation was concluded with the extracapsular technic.

Zonule.—Fragile zonules were encountered in about 15 per cent of the series; zonules with average resistance, in about 70 per cent, and zonules with above the average resistance, in about 15 per cent.

Types of Cataract.—The following types of cataract were encountered: immature senile cortical cataract, 25 cases; intumescent senile cortical cataract, 1 case; mature senile cortical cataract, 22 cases; hypermature senile cortical (shrunken) cataract, 1 case; nuclear cataract, 27 cases, and posterior cortical cataract, 24 cases.

Age Incidence.—The age distribution is indicated in the following tabulation:

Cases	*Age Period, Yr.*
0	20 to 30
2	30 to 40
7	40 to 50
12	50 to 60
54	60 to 70
21	70 to 80
4	80 to 90

Complications.—In 13 cases cataract was complicated by such conditions as preexisting glaucoma and uveitis.

Sex Distribution.—Of the patients, 43 were males and 57 females.

Number of Operations Performed.—A total of 111 operations was performed to achieve the results in these 100 cases. The following procedures were carried out: preliminary iridectomy, 1 case; preliminary operation for glaucoma, 3 cases; extraction with complete iridectomy, 38 cases; extraction with peripheral iridotomy, 62 cases; excision of prolapsed iris, 2 cases; discission, 2 cases; enucleation (glaucoma), 1 case; paracentesis, 1 case, and reattachment of the retina, 1 case.

Iridectomy and Iridotomy.—In 38 cases complete iridectomy was performed. In 3 of these cases an anterior synechia developed. In 3 cases the pillars of the iris were incarcerated, and in 32 cases the pillars were entirely free. In 62 cases an attempt was made to retain the round pupil by doing only a peripheral iridotomy before the cataract was removed. In 6 of these 62 cases a complete iridectomy was necessary before removal of the cataract. In 4 cases there was a small anterior synechia, and in 2 cases incarceration of the iris resulted. In 52 of the 62 cases

Case No.	Patient's Initials	Age, Yr.	Date of Operation	Resulting Visual Acuity	Refraction
1*	C. P.	70	5/14/40	20/30	+ 9.75 D. sph. ⊂ +2.00 D. cyl., axis 82
2	G. D.	64	9/10/40	20/25	+11.25 D. sph. ⊂ +2.00 D. cyl., axis 30
3	J. C.	60	10/22/40	20/20	+10.50 D. sph. ⊂ +1.25 D. cyl., axis 180
4	F. J.	78	11/12/40	20/30	+11.00 D. sph. ⊂ +1.50 D. cyl., axis 135
5	K. F.	73	11/12/40	20/25	+ 9.75 D. sph. ⊂ +0.75 D. cyl., axis 120
6	M. L.	74	11/26/40	20/100	+12.00 D. sph.
7	A. W.	75	1/ 7/41	20/20	+10.00 D. sph.
8	H. F.	66	1/14/41	20/20	+ 5.75 D. sph. ⊂ +1.00 D. cyl., axis 45
9	S. C.	73	1/14/41	20/30	+14.50 D. sph. ⊂ +2.00 D. cyl., axis 60
10	L. S.	62	1/21/41	20/25	+10.00 D. sph. ⊂ +2.25 D. cyl., axis 155
11	C. H.	71	2/ 3/41	20/30	+12.00 D. sph. ⊂ +1.00 D. cyl., axis 35
12	C. L.	45	2/ 4/41	20/30	+10.00 D. sph. ⊂ +1.25 D. cyl., axis 135
13	M. F.	81	2/18/41	20/40	+ 4.00 D. sph. ⊂ +3.00 D. cyl., axis 5
14	G. D.	65	4/22/41	20/20	+11.75 D. sph. ⊂ +3.00 D. cyl., axis 180
15	F. E.	65	4/22/41	20/20	+11.00 D. sph. ⊂ +0.50 D. cyl., axis 20
16	S. L.	65	4/29/41	20/25	+10.00 D. sph. ⊂ +0.50 D. cyl., axis 90
17	L. S.	64	4/29/41	20/20	+11.50 D. sph. ⊂ +0.75 D. cyl., axis 45
18	M. F.	81	4/29/41	20/50	+ 5.00 D. sph. ⊂ +3.00 D. cyl., axis 137
19	F. W.	64	5/ 6/41	20/30	+10.00 D. sph. ⊂ +1.00 D. cyl., axis 45
20	S. M.	44	5/ 6/41	20/20	+11.50 D. sph.
21	F. L.	61	5/13/41	H. M.†	+14.00 D. sph.
22	C. H.	71	5/13/41	20/20	+11.50 D. sph. ⊂ +2.00 D. cyl., axis 175
23	P. M.	68	5/20/41	20/40	+ 1.50 D. sph. ⊂ +4.50 D. cyl., axis 165
24	K. K.	57	5/20/41	20/50	+16.00 D. sph. ⊂ +1.25 D. cyl., axis 5
25	H. B.	68	6/ 3/41	20/20	+11.00 D. sph. ⊂ +2.00 D. cyl., axis 150
26	J. S.	52	8/19/41	20/20	+12.00 D. sph.
27	O. D.	65	9/ 7/41	20/20+	+12.00 D. sph. ⊂ +0.75 D. cyl., axis 135
28	R. I.	43	9/16/41	20/20	+13.25 D. sph. ⊂ +0.75 D. cyl., axis 25
29	M. H.	61	9/23/41	20/50	+10.25 D. sph. ⊂ +1.25 D. cyl., axis 180
30	S. L.	66	9/30/41	20/20	+11.50 D. sph. ⊂ +1.00 D. cyl., axis 90
31	S. E.	64	10/ 8/41	20/25+	+13.00 D. sph. ⊂ +1.50 D. cyl., axis 20
32	L. S.	75	10/28/41	20/20	+12.00 D. sph.
33	H. F.	66	10/28/41	20/30—	+ 5.75 D. sph. ⊂ +1.50 D. cyl., axis 180
34	E. F.	64	10/28/41	20/30	+12.00 D. sph.
35	S. E.	41	10/28/41	20/20	+14.50 D. sph. ⊂ +0.50 D. cyl., axis 25
36	K. F.	73	11/11/41	20/25	+10.00 D. sph. ⊂ +1.75 D. cyl., axis 15
37	R. C.	67	11/11/41	20/25	+12.50 D. sph. ⊂ +0.75 D. cyl., axis 10
38	M. McD.	65	11/25/41	20/20	+ 6.00 D. sph. ⊂ +1.25 D. cyl., axis 180
39	S. E.	64	12/ 9/41	20/30	+ 2.00 D. sph. ⊂ +1.75 D. cyl., axis 175
40	S. M.	62	12/16/41	20/25	+13.00 D. sph. ⊂ +1.50 D. cyl., axis 20
41	C. F.	46	1/ 7/42	20/20	+11.50 D. sph. ⊂ +1.50 D. cyl., axis 15
42	J. M.	60	1/13/42	20/20	+12.00 D. sph. ⊂ +1.00 D. cyl., axis 180
43	M. C.	67	1/20/42	20/30	+12.00 D. sph. ⊂ +1.25 D. cyl., axis 75
44	D. S.	76	3/ 3/42	20/50—	+ 6.50 D. sph.
45	E. L.	54	1/27/42	20/100 (later light perception only)	+ 8.00 D. sph.
46	M. McE.	66	3/ 3/42	20/20	+ 4.50 D. sph. ⊂ +2.00 D. cyl., axis 20
47	L. H.	78	3/ 3/42	20/20	+ 6.50 D. sph. ⊂ +1.75 D. cyl., axis 140
48	D. M.	61	3/10/42	20/20	+11.00 D. sph. ⊂ +2.25 D. cyl., axis 5
49	A. W.	75	3/10/42	20/20	+11.00 D. sph. ⊂ +1.50 D. cyl., axis 10
50	O. M.	38	3/17/42	20/25	+12.00 D. sph.
51	L. S	62	3/31/42	20/20	+10.25 D. sph. ⊂ +2.50 D. cyl., axis 15
52	K. K.	55	4/ 7/42	20/20+	+11.00 D. sph. ⊂ +1.50 D. cyl., axis 70
53	H. T.	62	4/ 7/42	L. P.	+ 9.00 D. sph.
54	M. E.	80	4/ 7/42	6/200	+11.00 D. sph.
55	R. F.	51	4/14/42	20/20	+11.00 D. sph. ⊂ +2.00 D. cyl., axis 155
56	K. F.	74	4/14/42	20/25	+10.00 D. sph. ⊂ +3.75 D. cyl., axis 170
57	M. T.	75	4/28/42	20/30	+ 6.00 D. sph.
58	H. M.	63	4/28/42	20/20	+12.00 D. sph. ⊂ +1.50 D. cyl., axis 165
59	L. H.	62	5/12/42	20/30	+11.00 D. sph. ⊂ +3.50 D. cyl., axis 175
60	S. M.	45	5/12/42	20/20	+11.50 D. sph. ⊂ +1.00 D. cyl., axis 155
61	M. C.	67	5/12/42	20/25	+12.25 D. sph. ⊂ +1.50 D. cyl., axis 50
62	G. M.	53	5/12/42	20/200	—8.00 D. cyl., axis 95
63	L. H.	61	5/21/42	20/20	+14.00 D. sph. ⊂ +0.25 D. cyl., axis 30
64	E. L.	64	5/21/42	20/20	+12.00 D. sph. ⊂ +1.75 D. cyl., axis 172
65	O. M.	38	5/36/42	20/25	+12.00 D. sph.
66	S. M.	61	5/27/42	20/25+	+13.00 D. sph. ⊂ +1.00 D. cyl., axis 175
67	E. C.	61	6/16/42	20/20	+11.00 D. sph. ⊂ +2.00 D. cyl., axis 25
68	S. W.	66	6/23/42	20/20+	+11.50 D. sph. ⊂ +0.50 D. cyl., axis 40
69	W. K.	69	8/11/42	20/20+	+11.00 D. sph. ⊂ +0.50 D. cyl., axis 120
70	F. A.	76	8/11/42	20/20—	+11.00 D. sph. ⊂ +2.00 D. cyl., axis 35
71	B. L.	62	8/11/42	20/20—	+10.50 D. sph. ⊂ +2.00 D. cyl., axis 30

* It was found after the paper had been written that in another case, with many complications before operation, the operation had been performed during the period. If this case were included, it would have taken the place of case 1, also a complicated one, and would not have materially altered the record.

† H. M. indicates ability to detect hand movements.

Case No.	Patient's Initials	Age, Yr.	Date of Operation	Resulting Visual Acuity	Refraction
72	F. M.	69	8/11/42	20/20	+12.00 D. sph. ⌢ +1.00 D. cyl., axis 25
73	M. O.	74	8/18/42	20/20	+ 9.00 D. sph. ⌢ +2.00 D. cyl., axis 175
74	L. S.	63	8/18/42	20/20	+10.25 D. sph. ⌢ +2.50 D. cyl., axis 15
75	B. G.	58	8/29/42	20/20	+14.00 D. sph. ⌢ +0.50 D. cyl., axis 85
76	A. D.	74	9/15/42	20/30	+11.50 D. sph. ⌢ +3.00 D. cyl., axis 90
77	S. G.	72	9/15/42	20/30	+10.00 D. sph.
78	E. O.	61	9/18/42	20/20	+10.50 D. sph. ⌢ +3.00 D. cyl., axis 140
79	B. J.	75	9/22/42	20/20	+11.00 D. sph. ⌢ +1.25 D. cyl., axis 50
80	J. S.	71	9/22/42	20/20	+11.00 D. sph.
81	G. M.	53	9/22/42	20/50	+ 0.50 D. sph. ⌢ —6.00 D. cyl., axis 100
82	P. F.	66	10/13/42	20/20—	+10.75 D. sph. ⌢ +1.00 D. cyl., axis 15
83	F. S.	51	10/13/42	20/20	+10.50 D. sph. ⌢ +1.00 D. cyl., axis 170
84	E. O'H.	67	10/13/42	20/20	+11.00 D. sph. ⌢ +1.00 D. cyl., axis 30
85	A. M.	60	10/13/42	20/30	+ 8.00 D. sph. ⌢ +4.00 D. cyl., axis 172
86	P. D.	57	10/20/42	20/25	+10.00 D. sph. ⌢ +1.50 D. cyl., axis 42
87	E. L.	64	10/20/42	20/20	+12.00 D. sph. ⌢ +1.25 D. cyl., axis 160
88	F. M.	69	10/20/42	20/20	+12.00 D. sph. ⌢ +1.00 D. cyl., axis 180
89	E. D.	69	10/20/42	20/20—	+11.50 D. sph.
90	M. L.	66	10/20/42	20/25	+10.75 D. sph. ⌢ +2.00 D. cyl., axis 45
91	F. H.	64	11/10/42	20/20	+ 8.00 D. sph. ⌢ +4.50 D. cyl., axis 10
92	C. H.	66	11/10/42	20/20	+ 8.00 D. sph. ⌢ +1.50 D. cyl., axis 15
93	S. L.	66	11/10/42	20/25	+10.50 D. sph.
94	E. G.	83	11/17/42	20/25	+10.50 D. sph. ⌢ +3.00 D. cyl., axis 20
95	S. F.	67	11/17/42	20/25	+ 4.00 D. sph. ⌢ +3.00 D. cyl., axis 165
96	E. O.	68	11/17/42	20/100	+10.00 D. sph.
97	E. C.	41	11/24/42	20/20	+ 6.50 D. sph. ⌢ +1.50 D. cyl., axis 45
98	H. N.	62	12/ 1/42	20/20	+13.00 D. sph. ⌢ +0.50 D. cyl., axis 100
99	D. C.	55	1/ 5/43	20/25	+ 3.50 D. sph. ⌢ —1.50 D. cyl., axis 5
100	R. C.	55	1/ 5/43	20/20+	+13.00 D. sph. ⌢ +1.25 D. cyl., axis 15

round, mobile pupils remained, without any synechia.

Loss of Vitreous.—In the 62 cases in which retention of the round pupil was attempted, the vitreous presented, with no loss in 3 cases and with loss in 4 cases. Of the 38 cases in which complete iridectomy was planned, vitreous presented, with no loss in 3 cases and with loss in 2 cases. Of the total series, vitreous presented with no loss in 6 cases and with loss in 6 cases. An analysis of the cases in which vitreous was lost follows.

In case 97 fluid vitreous seeped out directly after the incision had been made; the loss had no relation to the type of operation which followed. Stripping of the zonule was resorted to in this case, even in the face of the loss of fluid vitreous, because it seemed to be the only procedure which was feasible. The result was good. In case 62, because of severe and persistent vomiting due to sensitivity to codeine, prolapse of the iris developed forty-eight hours after the extraction. Loss of vitreous was experienced in the attempt to excise the prolapsed iris. In the same case, without the use of codeine, the other eye was operated on, with no loss of vitreous. In 2 complicated cases of glaucoma, in both of which previous operations had been performed, loss of vitreous occurred—in case 18 when the capsule ruptured and in case 21 during replacement of the iris pillars. In 2 cases (26 and 98) the loss of vitreous occurred unexpectedly during the actual delivery of the cataract in capsule. In both the hyaloid membrane seemed to be pathologically adherent to the posterior capsule of the lens and to follow the lens out in the shape of a cone.

Postoperative Condition of the Vitreous.—In general, pigment granules were enmeshed in the anterior portion of the vitreous and on the surface of the hyaloid membrane. In 28 cases the surface of the vitreous was flat and in its proper place behind the iris; in 45 cases there was a low mound at the border of the iris; in 18 cases the vitreous mushroomed through the pupil, and in 6 cases it was incarcerated. In 2 cases the vitreous formed a small mushroom through a discission opening, and in 1 case, through an iridotomy opening. The round pupil does not protect or hold back the vitreous during the extraction, but after healing has occurred, and when the round pupil is mobile and small, the iris helps to retain the vitreous better than the coloboma formed by the complete iridectomy.

Visual Results in Cases of Loss of Vitreous.—The patient with the fluid vitreous (case 97) had visual acuity of 20/20 with correction, and the patient with the prolapsed iris (case 62) visual acuity of 20/200 with a high minus cylinder. The latter had had considerable myopia before the cataract developed, and there were large areas of degeneration in the choroid and retina. In case 21, with increased intraocular tension complicating uveitis, vision was limited to perception of hand movements. In case 18, with apparent primary glaucoma complicating cataract, result-

ing vision was 20/30. In the other 2 cases (26 and 98), in which the vitreous appeared adherent to the posterior capsule of the lens, vision was 20/20 with correction.

Presentation of Vitreous Without Loss.—In 6 cases the vitreous presented at the time of actual delivery of the lens but none was lost. In 3 of these cases the vitreous receded and the eyes did well. The vitreous appeared mushroomed into the anterior chamber, but there was no inflammation and no increased tension, and the visual result was 20/20 in each case. In case 12 the vitreous became adherent to about one third of the incision, but there was no untoward development. In the other 2 cases (92 and 55) a secondary increase in intraocular tension developed. This was controlled by use of a 1 per cent solution of epinephrine bitartrate and a jelly containing 0.5 per cent epinephrine bitartrate over a period. In case 55 the patient is still under observation for control of the pressure.

Hemorrhage.—In 8 cases severe hypertension, not relieved by rest and medication, was present before and during the operation. In 17 cases there was embarrassing hemorrhage at the time of the operation, while in 8 of these 17 cases secondary hemorrhage occurred after operation. In 2 cases particularly severe hemorrhages were experienced, 1 being case 77, in which the blood was finally absorbed, after one month, with resulting vision of 20/30. In the other case (45) the patient was a particularly poor risk, with obesity, severe hypertension, nephritis and loss of one eye as a result of an injury in World War I. Six months' preparation of this patient was not sufficient to prevent hemorrhage. Vision with correction, five weeks after operation, was 20/100. In the sixth week a series of severe intraocular hemorrhages developed. Increased intraocular tension supervened, and it was necessary later to enucleate the eye.

Inflammation.—In 8 cases (68, 79, 92, 53, 21, 35, 42 and 47) there was evidence of uveitis before operation. Of these, postoperative inflammation developed in 5 cases, while in 3 cases (68, 35 and 47) the eye remained free. In 10 cases uveitis or iridocyclitis which followed operation was controlled with difficulty. Of these, a secondary, or adventitious, membrane formed over the surface of the vitreous, requiring discission, in 1 case (63), while iridotomy was necessary in another (case 1). A cyclitic membrane developed in 2 cases with complications (21 and 53), and vision was not restored. In both these cases severe uveitis and secondary increase in intraocular tension were present before the operation for cataract, and iridectomies had been performed by other surgeons.

Inflammation arose in 6 cases without previous complication—in 3 cases after extracapsular delivery following the attempted intracapsular procedure and in 3 cases after intracapsular delivery. In 1 of the latter cases (26) vitreous had been lost.

In case 1 a recent infection of the respiratory tract had existed, and purulent endophthalmitis developed. The use of sulfadiazine and nonspecific foreign protein resulted in preservation of the eye after secondary rise of tension, iris bombé and iridotomy by transfixion of the iris, with final useful vision of 20/30.

Glaucoma.—In 2 cases (13 and 18) primary glaucoma, and in 2 cases (21 and 52) severe uveitis with increased intraocular tension, complicated cataract before operation. In the first 2 cases a preliminary operation was performed, and final vision was 20/50 and 20/30 respectively, while in the last 2 cases only light perception remained.

Of 6 cases in which there was no evidence of glaucoma before operation, the intraocular tension rose in 3 (cases 1, 92 and 55) after the intracapsular operation, and in 2 cases the increase in tension was temporary and was controlled by medication, after which no treatment was necessary. In 1 case (1) iridotomy by transfixion of the iris gave satisfactory results. Of the 3 cases of extracapsular extraction after attempted intracapsular delivery, repeated paracentesis satisfactorily relieved the condition in case 38, sclerectomy and peripheral iridectomy were necessary in case 2 and enucleation was finally required in case 45.

Behavior of the Patient During and After Operation.—Sedation, local anesthesia and induction of akinesia were employed in all cases of the series. In 18 cases the behavior of the patient at the time of operation was embarrassing, through lack of cooperation, inability to maintain a satisfactory position of the eyes, coughing, movement of the head, rigidity, inability to relax or other nervous manifestations. In at least 6 of these cases induction of general anesthesia would have been dangerous because of hypertension and insufficient cardiac reserve. In 6 cases an irrational condition developed after the operation, in 1 (case 77) of which a serious hemorrhage and prolapse of the iris resulted.

Detachment of the Choroid.—In no case was ophthalmoscopic inspection of the fundus made directly after removal of the cataract. In the early period of convalescence, the anterior segment was carefully inspected with the aid of an

oblique pencil of light from a self-luminous flashlight. Only toward the end of the twelve day period of hospitalization was ophthalmoscopic examination made. Detachment of the choroid was found at this time in 5 cases, in which it was associated with the following conditions: in case 5, with continued leakage from the incision, the central suture of which had loosened, with resuture on the tenth postoperative day; in case 92, with delayed reformation of the anterior chamber, anterior synechia and secondary increase of intraocular tension, which developed later; in case 24, with chondrodystrophia, in which the sclera was particularly rigid and the retina became detached later, with complete reattachment after operation (to be described in the next section); in case 18, with glaucoma, rupture of the capsule and slight loss of vitreous, and in case 26, with loss of vitreous. In each of these 5 cases the choroid became reattached completely after varying periods, the longest (case 24) being five months.

Detachment of the Retina.—In case 24 detachment of the retina developed. This case was a particularly interesting instance of osteochondrodystophy with general maldevelopment, in which detachment of the retina of the right eye followed an extracapsular extraction by a surgeon in a distant city. The patient was referred to me for operation for reattachment of the retina in this eye. The entire lower half of the retina was detached in bullous form. No tear was detected. Extensive surface diathermy was used over the sclera, which proved to be at least 1.5 mm. thick. Penetrating diathermy was also employed, and, finally, two trephine openings were made for drainage. Complete reattachment of the retina was obtained in three months, with a resulting satisfactory visual field and central vision of 20/50 with correction. I removed the cataract from the left eye by intracapsular extraction, with complete iridectomy. Detachment of the choroid developed and was followed later by extensive detachment of the retina. An operation was performed on this eye similar to that described for reattachment of the retina in the right eye. A similar, entirely successful result was obtained. I have operated on a total of 5 aphakic eyes with detached retina, and this is the only case in which I have been successful.

Astigmatism After Operation.—In 15 per cent of the cases no correction was required for astigmatism; in 13 per cent there was no to 1 D. of astigmatism, or 1 D. or less in 28 per cent; in 38 per cent there was 1 to 2 D. of astigmatism, or 2 D. or less in 66 per cent, while in 16 per cent there was 2 to 3 D. of astigmatism, in 9 per cent 3 to 4 D. and in 5 per cent 4 D. or more; in 4 per cent the patient was unable to estimate the astigmatism.

The average strength of sphere accepted was + 10.5 D., and the average strength of cylinder, + 1.50 D.

Resulting Visual Acuity.—In 5 per cent of cases vision was 20/20 + ; in 44 per cent, 20/20, or 20/20 or better in 49 per cent; in 4 per cent, 20/20 —; in 19 per cent, 20/25; in 14 per cent, 20/30, or 20/30 or better in 86 per cent; in 2 per cent, 20/40, or 20/40 or better in 88 per cent; in 5 per cent, 20/50; in 2 per cent, 20/100; in 1 per cent, 20/200, and in 4 per cent, less than 20/200.

Visual Acuity of 20/100 or Less: In case 6, with visual acuity of 20/100, and in case 54, with an acuity of 12/100, central chorioretinopathy was due to senile degeneration. In 2 cases (21 and 53) in which uveitis and secondary increase of intraocular tension preceded the cataract, vision was limited to perception of hand movements. In case 45, in which vision of 20/100 was obtained five weeks after operation, severe hemorrhagic glaucoma later developed, with unbearable pain and reduction of vision to perception of light. Finally, enucleation was necessary. In the 1 case (62) in which vision was 20/200 degenerative myopic choroioretinopathy existed.

SUMMARY AND CONCLUSIONS

The system of manipulations used in intracapsular extraction of cataract with intact zonule is briefly described again, and the statistics of results in 100 consecutive cases of intracapsular extraction, representing every case in which the operation was attempted, are given. The results substantiate claims for the safety and rationale of the procedures employed. Two years ago it was stated that the manipulations of appositional suturing after the corneal incision, the lifting of the corneal flap and the application of the three efforts (the preliminary pressure; the pressure, traction and rotation, and the stripping of the zonule) were all feasible. Now it is reported that they are conservative and desirable. A series of observations made before and after each maneuver of intracapsular extraction with use of the indicated manipulation is worth while. The effect of each maneuver was studied with respect to the accomplishment of its purpose and the event of any complication resulting from or occurring independent of the maneuver. A maneuver which was ineffective in any particular case was not repeated. A variety of maneuvers is possible from combinations of those which have been described. They have all proved satisfactory in their application to the cases in which

intracapsular extraction was attempted and have been applied even when the zonule was resistant. The future may indicate changes in this system of intracapsular extraction of cataract as applied to lenses with intact zonules, but so far it has been satisfactory.

780 Park Avenue.

DISCUSSION

Dr. C. A. Clapp, Baltimore: Has Dr. Kirby any pathologic specimens showing that the zonular fibers are replaced by a membrane? Certainly, in all my sections of eyes I have never seen such a condition occur. It is quite possible that this condition may be a congenital anomaly; however, I have never encountered it.

Dr. John Green, St. Louis: In private discussion among members of the society, the point has been raised that elevation of the corneal flap and eversion by means of the central suture might induce keratitis or other permanent changes in the cornea. I have been using this central suture for eversion for the last five years. My experience bears out Dr. Kirby's contention that the maneuver is harmless. I have never observed any corneal complication that could reasonably be ascribed to this procedure.

Dr. Thomas D. Allen, Chicago: I did not give much consideration to postoperative peripheral synechiae until I began to use the contact glass routinely in postoperative examination. I did not realize how frequent is the postoperative occurrence of peripheral synechiae, a condition which, it seems to me, predisposes to glaucoma. Has Dr. Kirby used the contact glass in postoperative examinations? How does he make the diagnosis of peripheral synechiae?

Dr. Daniel B. Kirby, New York: In reply to Dr. Clapp, it is well recognized by such men as Troncoso, Duke-Elder and Goldsmith that in living eyes, and in fresh eyes which have recently been removed from the body, there is a definite membrane which stretches between and over the zonular fibers. I, personally, have no doubt of the existence of such a membrane.

In answer to Dr. Green, I can definitely state that elevation of the flap is a conservative maneuver, and I have never seen any complication due to it alone. I have even lifted the flap after the cataract was removed. That can perhaps be said to be a more hazardous procedure, but it has never resulted in any complication. I observe the position of the iris, and if it is not incarcerated between the lips of the wound, I do not employ the iris repositor, for I know that use of the miotic will draw the iris into the anterior chamber. The precautions used in the prevention of anterior synechiae are (1) avoidance of trauma to the iris and the endothelium of the cornea, (2) rapid closure of the anterior chamber by efficient suturing and (3) drawing of the iris into its proper place by use of a miotic.

I have used the contact glass in the examination of patients after convalescence, but not as a routine measure. I think one can tell by the plane of the iris whether it is near the plane of the incision. I can definitely state that anterior synechiae were present in only 4 per cent of cases in which vitreous was not lost. In 1 case glaucoma developed, but with use of miotics and agents for contraction of the blood vessels, the tension was brought under control. In 5 previously reported cases anterior synechiae accompanied incarceration of vitreous after loss of vitreous.

BOWEN'S DISEASE OF THE CORNEA

CARLOS WESKAMP, M.D.
Professor of Ophthalmology, Universidad Nacional del Litoral
ROSARIO, ARGENTINA

In 1912 Bowen[1] first described in detail a disease of the skin which he called precancerous dermatosis. It is characterized by the presence of lenticular or nummular spots which coalesce to form asymmetric plaques of various sizes. These plaques may be squamous or scabby, papular or wrinkled. Sometimes they regress and assume the appearance of atrophic spots. They may be a shade darker than the skin or may vary from pale pink to dark pink or copper red. Their outline is sharp; there is no halo of congestion. When the scab is removed, a wet, pink surface appears, which may be smooth, granular or, more rarely, warty. But soon new layers cover the area.

The disease is extremely chronic and slowly progressive. Cases in which the disease developed over twenty, thirty or even forty years have been recorded. Histologically, the lesion has the appearance of an epithelioma composed of dyskeratotic cells which have not yet ruptured the basement membrane—"intraepithelial epithelioma". It persists unaltered in this phase for a long time, but at last it becomes a true epithelioma, breaking through the basement membrane, infiltrating the underlying tissues and metastasizing. It is said, however, that in Bowen's disease metastasis may occur before the lesion becomes a true epithelioma.

In 1921 Jessner[2] reported the first case of the lesion observed on a mucous membrane. Since then several cases in which Bowen's disease involved the skin and mucous membranes have been described, and at present this disease is well known to dermatologists.

Before Bowen's report, Darier had described several diseases, such as psorospermosis vegetans, Paget's disease (osteitis deformans) and molluscum contagiosum. Common to all were cells of a certain type, which he called dyskeratotic. Thus was created the group of dyskeratotic diseases. When Bowen described the disease that now bears his name, Darier[3] included it in this group, as dyskeratotic cells were present. Two dyskeratotic diseases, Paget's and Bowen's, evolve into cancer after a considerable period. This peculiarity has given rise to a subgroup, known as precancerous dyskeratosis, or epitheliomatous dyskeratinization. But some authors have maintained that the term "precancerous" is not applicable and have asserted that the lesions are true epitheliomas from the beginning. The fact that the lesion does not break through the basement membrane to infiltrate the underlying tissues simply means that the epithelioma is in a stage of evolution; if sufficient time is given, however, it will assume the infiltrative character of all epitheliomas.[4]

In a review of the ophthalmic literature, I did not find the report of any case of Bowen's disease in which the cornea was involved until 1942. In February 1942 McGavic[5] recorded 5 such cases; a year later Wise[6] referred to another case. Ash and Wilder,[7] in a paper dealing with epithelial tumors of the limbus, mentioned 4 cases in which the structure of the lesion was similar to that of Bowen's dyskeratosis. Thus, only two reports of Bowen's disease of the cornea have been made previously, and the presentation of my case is the third.

In McGavic's cases 4 patients were women, of whom 3 were over 60 and 1 was 46 years of age. The age of the only male patient was not given. Wise's case was that of a man aged 62. In the present case the patient was a man aged 56. One may say that the disease is fairly equally distributed between the sexes (57 per cent women and 43 per cent men), with a slight predominance of women. But in both men and women the disease appears after the forty-fifth year.

With respect to the presumable cause, in 3 of McGavic's cases trauma or inflammatory lesions

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Read at the monthly meeting of the Sociedad de Oftalmología del Litoral, in May 1943.

1. Bowen, J. T.: J. Cutan. Dis. **30**:241, 1912.
2. Jessner, M.: Arch. f. Dermat. u. Syph. **134**:361, 1921.
3. Darier, J.: Ann. de dermat. et syph. **5**:449, 1914.
4. Rousset, J.: Les dyskératinisations épithéliomateuses, Paris, Masson & Cie, 1931.
5. McGavic, J. S.: Am. J. Ophth. **25**:167, 1942.
6. Wise, G.: Am. J. Ophth. **26**:167, 1943.
7. Ash, J. E., and Wilder, H. C.: Tr. Am. Acad. Ophth. (1941) **46**:215, 1942.

of the cornea existed prior to the dyskeratotic changes. In his other 2 cases there had been no previous corneal disturbance. In the case presented by Wise and in that which will be described here no corneal lesion was present before the growth appeared.

normal cornea. The whole lesion had the appearance and the grayish color of ground glass except at the edges, near the limbus, where it was pinkish. On the surface, little globular, translucent excrescences of gelatinous tissue were observed. The pinkish color was given by fine blood vessels arising from the limbus and invading that area of the plaque. They stopped

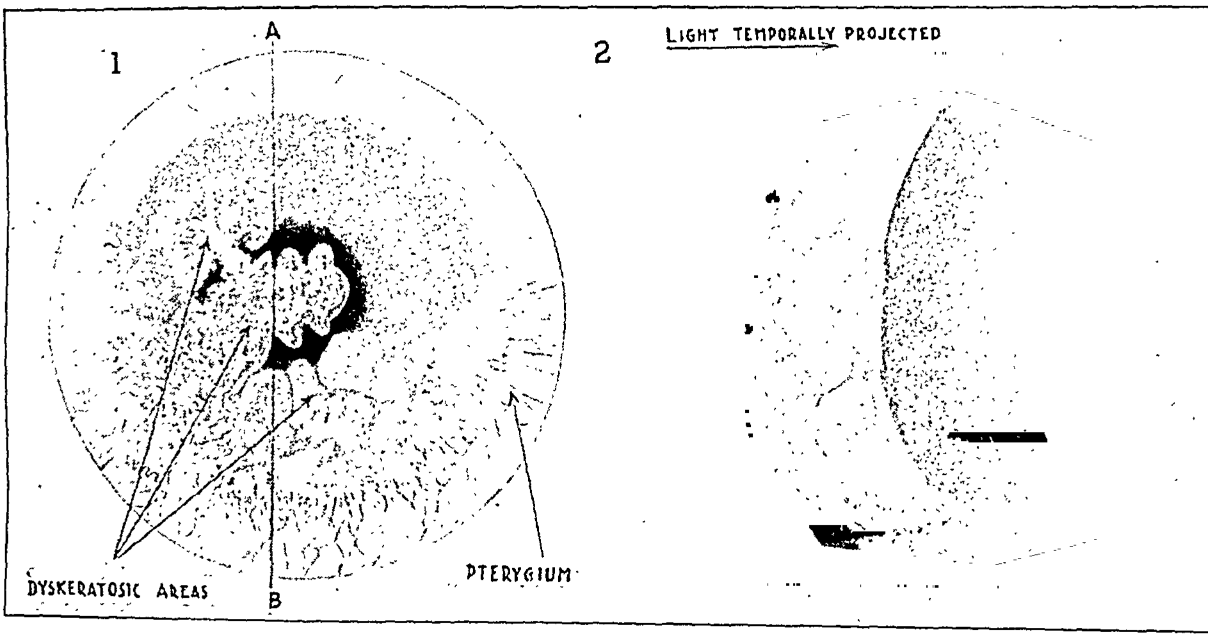

Fig. 1.—(*1*) Drawing of the lesion on the right cornea, *AB* being the axis of a semischematic cut, a photograph of which (*2*) was obtained with the slit lamp.

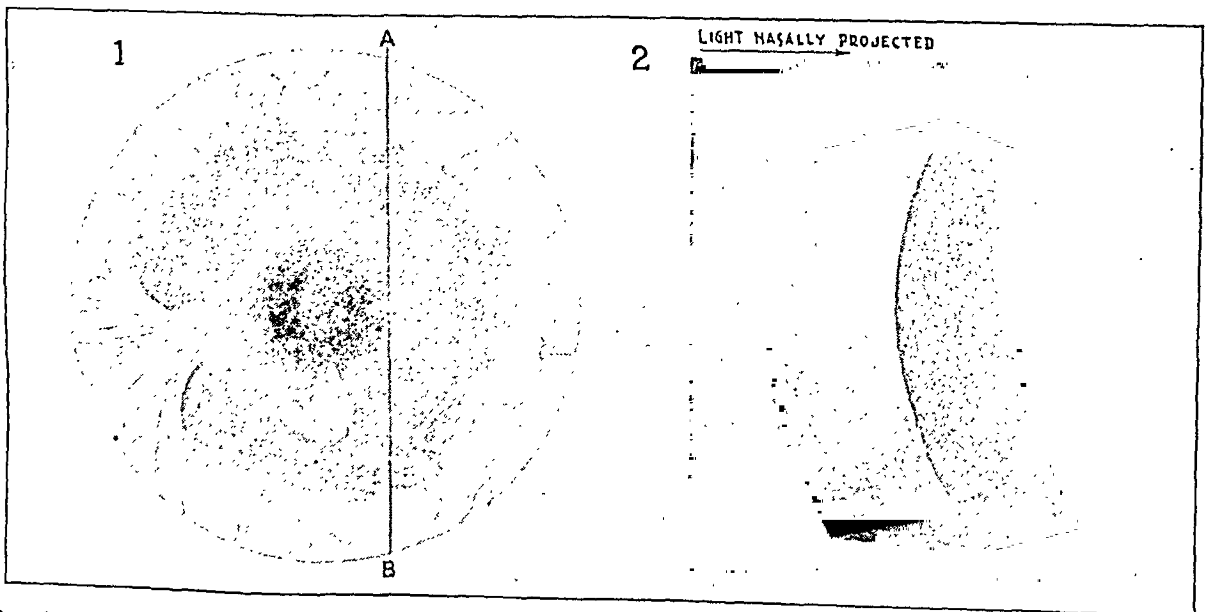

Fig. 2.—(*1*) Appearance of the lesion on the left eye, *AB* being the axis of a semischematic cut, a photograph of which (*2*) was obtained with the slit lamp.

REPORT OF A CASE

On Nov. 20, 1942 a healthy-looking man aged 56 came to my private clinic with a condition of the cornea which had appeared three years before in the right eye and more recently in the left eye.

Gross Appearance.—The cornea of the right eye presented a plaque formed by the coalescence of numerous small, rounded spots. The process was slowly progressive but not ulcerative. It covered the lower half of the cornea and involved the pupillary field almost completely. Subsequently, vision was reduced to ability to count fingers at 3 meters. The plaque had a scalloped edge, which ended abruptly at the shortly after penetrating the plaque 2, 3 or 4 mm., before returning to the limbus. The plaque was vascularized only in the parts lying near the limbus. The vessels were dendritic and ran within the epithelium, without passing into the stroma at any point. The corneal tissues around the plaque were normal, and the limbus surrounding the normal portion of the cornea showed no vascular reaction. Examination with the slit lamp revealed that the lesion was lying in the epithelium, the parenchyma being normal.

A second examination revealed a pterygium at the inner angle of the eye, which advanced a few millimeters onto the cornea (fig. 1). Sensitivity of the cornea was reduced in the pathologic area only.

In the left eye I encountered three plaques on the cornea, formed, like the one previously described, by coalescence of numerous small spots. One of the plaques lay on the vertical meridian, immediately beneath the pupil. The other two were at the periphery, between 4 and 5 o'clock. Perikeratic, as well as intraepithelial, vascularity was almost entirely absent. The whole lesion resembled the plaque in the right eye, the only difference being that it was less vascularized (fig. 2).

According to the patient's statement, light usually did not disturb him much, but he had periodic attacks of photophobia and tearing. He did not complain of spontaneous or of provoked pain.

General Physical Examination.—Nothing significant was observed except for the presence of whitish plaques on the mucous membrane of the lower lip. The patient told me that they had been treated with solid carbon dioxide three or four times, but always reappeared. A specimen from one of these plaques was sent to the pathologist, Dr. Anibal Castañe, of the department of dermatology of the faculty with which I am associated. He reported as follows:

"The epithelium covering the semimucous membrane of the lower lip showed a thick, horny layer and a stratum granulosum formed of five or six layers. The epithelium owed its thickness to the presence of uniform cells. No cells similar to those characteristic of dyskeratosis were present. No atypical mitotic figures or polymorphism was observed. The corpus mucosum of Malpighi and the generative layer showed no important change. The upper part of the corium and the papillary layer of the dermis were sclerosed and invaded by lymphocytes and by vessels, which were congested.

"One may conclude that the semimucous membrane of the lower lip had acquired features similar to those of the skin of the hand or foot; that is, a stratum granulosum and a thick horny layer, which normally do not belong to the lip. Besides, there were sclerosis and lymphocytic infiltration. All these features suggest classification of the lesion as leukoplakia of the lip."

The skin presented no lesion of any kind; it appeared perfectly healthy.

Since the corneal lesion that interfered with vision was confined exclusively to the epithelium, a superficial excision was made. The wound healed in a few days, the cornea being clear and transparent. The excised specimen was fixed in Bouin's solution and embedded in paraffin. Sections were stained by several methods.

Microscopic Study.—Under low magnification, the epithelium appeared of varying thickness. In some places it was many times as thick as normal, twenty or more cells being counted, and in the thinner portions only six or seven cells were seen, a number which was also above the normal. The thicker parts corresponded to the excrescences which were clinically evident on the corneal surface. The epithelium covering the affected area ended abruptly at the normal epithelium. It did not stain uniformly but appeared to be covered with faded blotches. The epithelial cells were not normally arranged in layers but were irregularly intermingled. Only cells bordering on the basement membrane retained their palisade arrangement. Bowman's membrane appeared intact throughout, and the underlying parenchyma was also normal. Some clear, large cells were scattered throughout the epithelium. Several vessels were discernible (fig. 3).

Fig. 3.—Panoramic photomicrograph, taken with low magnification. The epithelium is irregularly thickened. The staining qualities are also irregular, as some areas appear dark and others clear.

With high magnification the anarchy in the shape and arrangement of the epithelial cells could be appreciated. The cells varied in size to an extraordinary degree: Some were small, while others were many times as large as normal. Some cells stained well and others faintly. They were not in layers but were arranged in disorderly fashion. In several places they were concentrically arranged, with the well known appearance of epithelial pearls. Certain cells presented atypical mitotic figures. Their nuclei assumed various sizes and shapes; some of them were elongated and others rounded or clumped. Some nuclei stained well, while others remained pale.

Certain cells attracted attention because of their paleness and enormous size, which was many times that of the basal cells. They had no tonofibrils. One encountered them among the basal cells, as well as in the middle portion or on the surface of the epithelium Wherever they lay, they were remarkable for their enormous size and for their peculiar appearance.They occurred alone or in small groups, but they were always connected with their neighboring cells by intercellular bridges, which were clearly demonstrable. The nucleus of these cells was irregular in shape, being rounded elongated or clumped. It was enormous and contained one, two or three nucleoli. Each nucleus was partially or totally surrounded by a vacuole, which pushed the protoplasm to the periphery. The cytoplasm was finely granular and finely vacuolated. It was condensed at the periphery, so that the cell was sharply outlined. These cells were of the dyskeratotic type.

The intraepithelial vessels had their own walls. Some of them appeared to be surrounded by an infiltrate of cells and plasmalymphocytes. In several places the perivascular connective tissue had undergone hyaline degeneration. Isolated hyaline "herds," arising perhaps from the perivascular connective tissue, were also noted. The cells around the vessel had the appearance of a papilla in transverse section (figs. 4 and 5 *A*). Bowman's membrane was unruptured; only at certain points was it penetrated by vascular buds. The basal cells, however, did not invade the underlying stroma at any point, but retained their orderly arrangement (fig. 5 *B*). The underlying stroma was normal, but at certain places, immediately beneath the epithelium, slight infiltration with plasma cells and lymphocytes was present (fig. 5 *C*).

The lesions described were confined exclusively to the epithelium of the cornea in the left eye, but in the right eye they also involved the epithelium of the nearest portion of the conjunctiva to a slight extent.

All these changes, that is, the lack of orderly arrangement of the cells, their diversity in size and shape, their monstrosities, the atypical mitotic figures and the variation in staining properties, gave the lesion the appearance of an epithelioma. But two outstanding features marked the difference between this growth and a true epithelioma: First, the basement membrance was not ruptured at any point, all the cellular changes taking

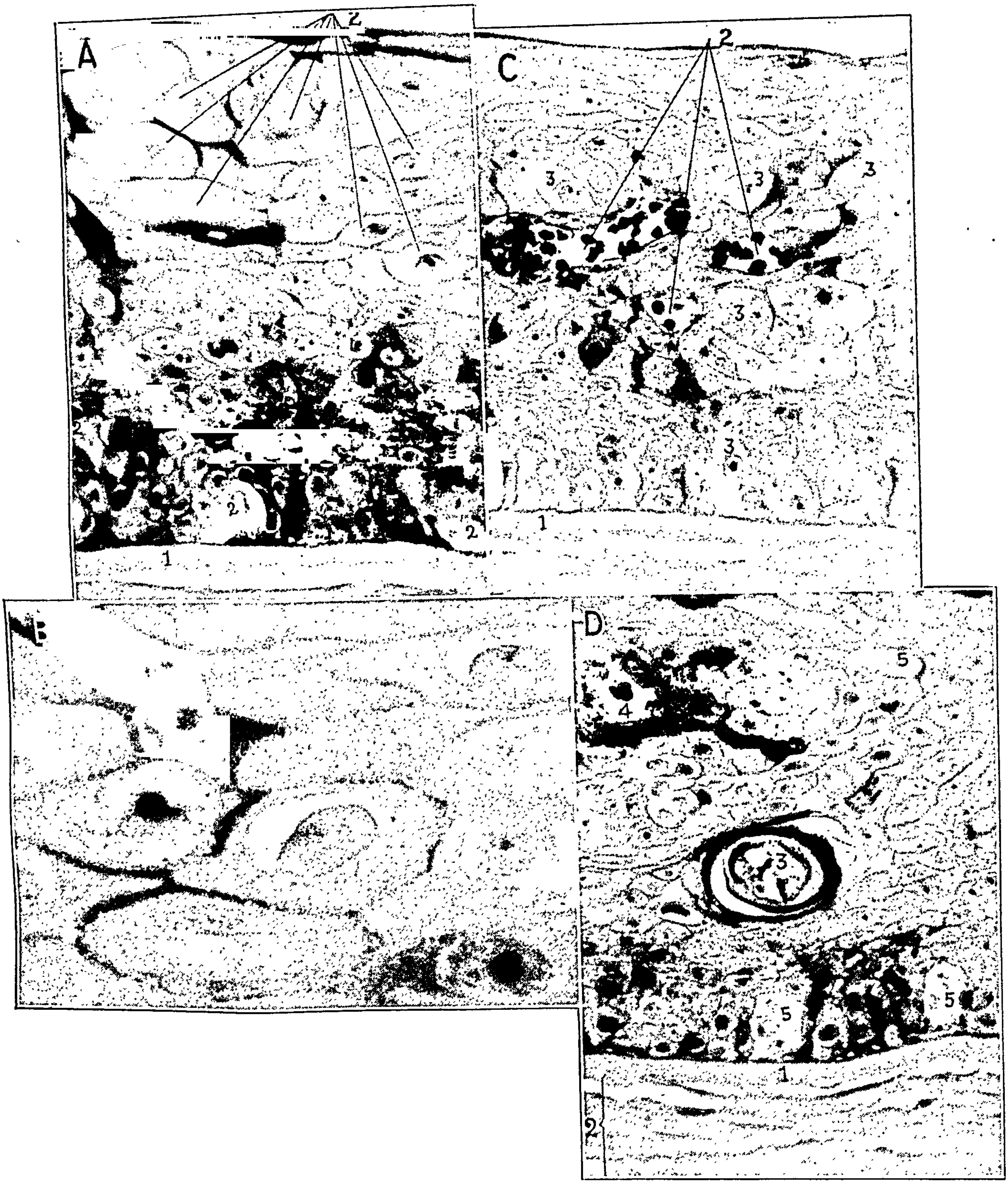

Fig. 4.—*A*, thickening of the epithelium, due to the presence of numerous cells, disorderly arranged ai varying in size and staining characteristics. *1* indicates the basement membrane, which is intact, and *2*, monst cells. The cytoplasm is hypochromatic, condensed at the periphery, finely granular and finely vacuolate Intercellular bridges are clearly seen. The nuclei are large, vary in shape and contain more than one nucleol The nuclei are surrounded by a vacuole (dyskeratotic cells of Bowen's type).

B, high magnification of the monster cells shown in *A*, with large nuclei of various shapes, containing nucle and surrounded by a vacuole. The protoplasm is granular and vacuolated. Intercellular bridges are discernib

C, hyperplastic epithelium, made up of cells which show great variation in size and are disorderly arrange *1* indicates Bowman's membrane, which is normal; *2*, capillary vessels with red corpuscles in their lume and *3*, some dyskeratotic cells.

In *D*, *1* indicates Bowman's membrane; *2*, the corneal parenchyma, *3*, an epithelial pearl; *4*, a capillary ves surrounded by hyaline masses derived from degenerated perivascular connective tissue, and *5*, some dyskeratotic cel

place within the epithelium, and, second, there were dyskeratotic cells with intercellular bridges. All the histologic changes encountered in the corneal lesion were similar to those observed in lesions of Bowen's disease of the skin

In my opinion, superficial excision is the treatment of choice when dyskeratosis is suspected.

It is interesting to note that the corneal lesion was the only manifestation of Bowen's disease in this case, the skin being healthy.

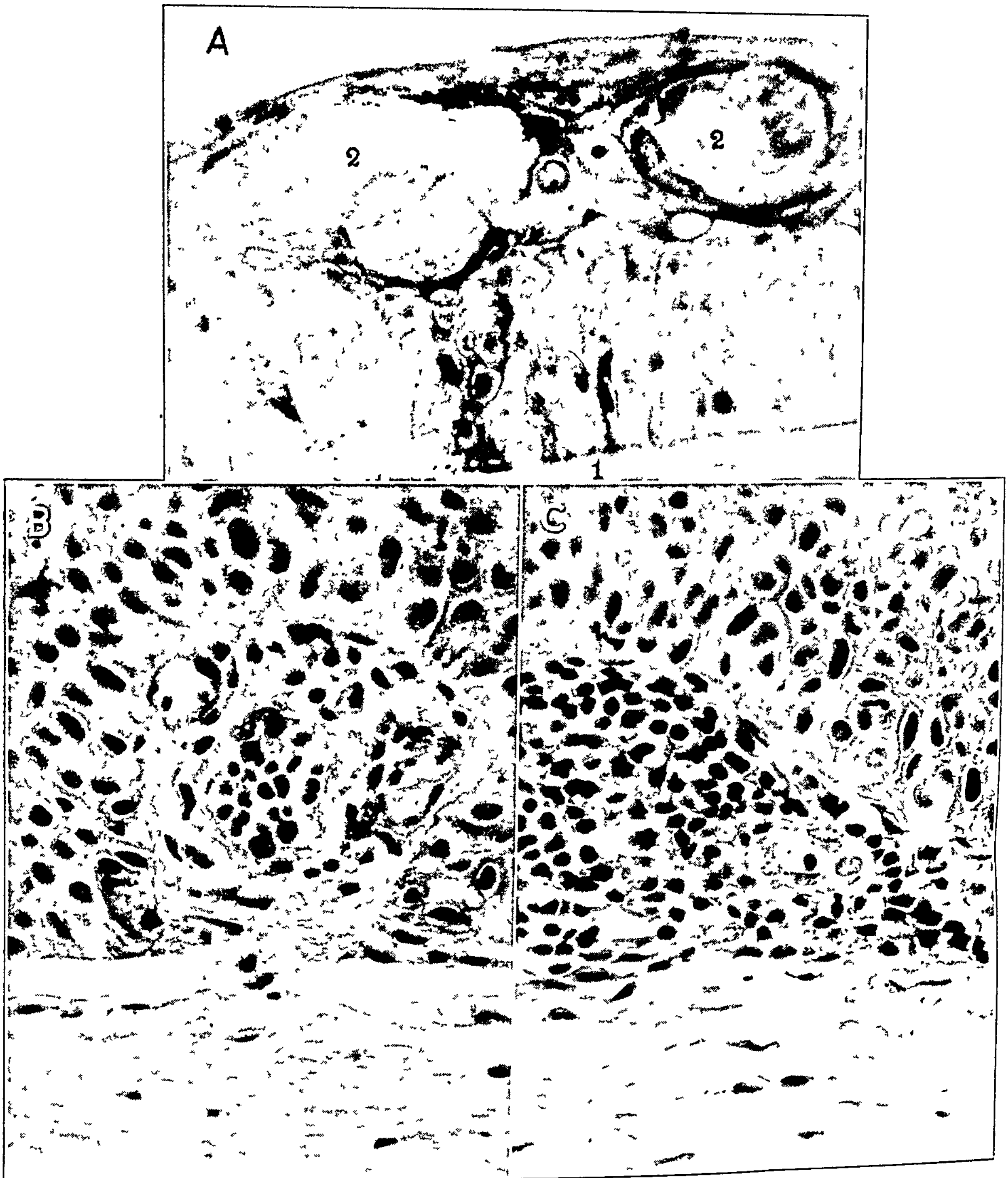

Fig. 5.—*A*, photomicrograph, showing some of the cellular features described in the preceding figure *1* indicates the basement membrane, which is intact, and *2*, hyaline "herds" *B*, Bowman's membrane penetrated and disrupted by a vessel. The perivascular cells surround the vessel, arranged like a papilla. The basement cells do not invade the stroma. *C*, subepithelial infiltrate The basement membrane is disrupted, but the epithelium does not invade the underlying tissues

Again, in the present case, it must be added that although the area of excision involved almost one-half the cornea, the postoperative course was excellent. In a week the wound was healed and the cornea perfectly transparent. When the patient was examined eleven months later, no sign of recurrence was present. Vision was recorded as 2/3 with Snellen's chart.

COMMENT

A diagnosis of Bowen's disease of the cornea can be made only through a histopathologic study of the lesion. The pathologic process involves only the epithelial layers of the cornea Therefore, when Bowen's disease is suspected.

a specimen for biopsy can be taken without fear of damage to the eye. The following clinical features may lead to a tentative diagnosis: the slow course of the disease, with little subjective trouble, and the appearance of nummular or lenticular spots in the epithelium, which enlarge slowly and coalesce to form escalloped patches of varying size. These end abruptly at the normal portion of the cornea. The lesion has the grayish color of frosted glass, but in some vascularized areas it becomes salmon colored. On its surface globular, translucent, gelatinous excrescences are observed. Vascularity of the cornea is scant, and the vessels are intraepithelial; interstitial vessels were not encountered in the present case. In this case the vessels were dendritic and stopped after penetrating the lesion a few millimeters, before returning to the limbus. On examination with the slit lamp one could see that the lesion lay above Bowman's membrane and that the globular excrescences of the epithelial surface were due to thickenings of the epithelial layers. The parenchyma maintained its appearance and normal transparence throughout.

Surgical therapy is effective, as the lesion may be totally removed without further complications and a clear cornea left. It is interesting to note that in the present case the ocular lesion was the only manifestation of Bowen's disease. Neither the skin nor the mucous membrane was involved.

Since a specimen for biopsy can be taken from the surface of the cornea without evil consequences to the patient, histologic study should be undertaken more often when Bowen's disease of the cornea is suspected clinically. The benefit to the patient will be greater, as early diagnosis aids in recovery, before the growth undergoes malignant change. Personally, I think that many new cases would be detected if biopsy of specimens from the cornea were made more often.

SUMMARY

Some dermatologists classify Bowen's disease as precancerous dyskeratosis; others consider it as cancerous from its onset.

In the case of Bowen's disease reported here, a man aged 56 presented on each cornea patches of grayish, ground glass appearance, formed by the coalescence of numerous minute, rounded spots. On the surface occurred little translucent protrusions of gelatinous tissue. The parts of the plaque near the limbus were somewhat vascularized. The lesions were superficial and ended abruptly at the normal portion of the cornea. Histologic examination revealed that the lesion was an epithelioma which had developed within the epithelium, without breaking through the basement membrane. Large, clear cells with irregular nuclei and cells of the so-called dyskeratotic type, exactly as they appear in cases of Bowen's disease of the skin, were demonstrable.

The skin was normal, but in the mucous membrane of the lower lip an area of leukoplakia was present.

As the corneal lesion was superficial, it was totally excised. Removal of the area left a clear cornea. Vision improved from ability to count fingers at 3 meters to 2/3 with Snellen's chart.

Laprida 1159.

DIAGNOSTIC VALUE OF MONOCULAR OCCLUSION

KENNETH L. ROPER, M.D., AND ROBERT E. BANNON, B.S.
HANOVER, N. H.

The ophthalmologist frequently fails to give his patient comfortable binocular vision in spite of the fact that he has adequately corrected errors of refraction and motility and has eliminated the possibility of ocular disease and inflammation. The reason for this may be that some disorder of binocular vision is at fault. Of interest, therefore, is a report of the results obtained in a series of cases studied at the Dartmouth Eye Institute in which monocular occlusion was used for the purpose of determining whether binocular anomalous vision was at fault.

The chief disorders affecting the comfortable and efficient cooperation of the two eyes in binocular vision are heterophoria, accommodation-convergence imbalance and aniseikonia. Binocular single vision is not present in cases of strabismus, and symptoms in such cases cannot be due to disorders of the binocular processes. On the contrary, correction of the deviation and restoration of binocular vision may result in production of eyestrain of binocular origin, although the patient previously had no symptoms because he had been suppressing the image of the deviating eye. In fact, monocular suppression, which is quite analogous to monocular occlusion, may be nature's way of dealing with binocular defects which make binocular vision uncomfortable.

If binocular vision is interrupted by the occlusion of one eye, then such causal factors of eyestrain as heterophoria, disturbances of the accommodation-convergence relationship and aniseikonia have been eliminated, and the neuromuscular mechanism concerned with binocular vision is relieved of many fine and exacting adjustments. Relief from symptoms during a period of monocular occlusion, which eliminates the disorders of binocular vision aforementioned, should lead one to believe that some binocular difficulty is present. It must then be determined what binocular factor is at fault. Occlusion studies sometimes do more than establish the cause of the patient's symptoms; they may point to the advisability of adopting the practice as a therapeutic measure.

Marlow has contributed most to the literature on monocular occlusion. He claimed to have begun the use of monocular occlusion for diagnostic purposes as early as 1894,[1] although his first paper did not appear until 1897,[2] when a patient he had been treating complained of diplopia after having had one eye bandaged for a week. The patient had never had double vision before, and Marlow expressed the belief that monocular occlusion might be a new aid in bringing out latent muscular deviations.

Marlow published a monograph [3] on monocular occlusion in 1924, with statistics on 700 cases. It was on the results in these cases that he based the value of his test. He used monocular occlusion primarily to uncover latent heterophoria. His procedure was to cover the nondominant eye, using either a ground glass spectacle lens or black court plaster on the spectacle lens. Marlow insisted that monocular occlusion had much greater value when the eyes were dissociated for from three to seven days.[4]

In 1938,[5] after using the test for over forty years, Marlow drew the following conclusions from his experience with the prolonged occlusion test: He expressed the belief that heterophorias and disturbances in duction could all be accounted for on an evolutionary basis, and by no other conceivable hypothesis, and that the evolution of the race and the development of the individual concur in furnishing an explanation at least for the lateral deviations, particularly exophoria. He stated the opinion that conditions such as overdevelopment, faulty insertion or abnormal length of a muscle, declinations (as described by Stevens), aniseikonia and paresis are underlying anatomic states rather than causes.

Many eminent ophthalmologists [6] have used the occlusion test with good results and have

Read before the Section of Ophthalmology, New York Academy of Medicine, Jan. 17, 1944.

1. Marlow, F. W.: The Technique of the Prolonged Occlusion Test, Am. J. Ophth. **15**:320-323 (April) 1932.
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(Footnote continued on next page)

written favorably about it. When Fuchs [7] visited the United States, he was favorably impressed with this test, having observed its use by a number of American ophthalmologists. Worth [8] listed occlusion as one of the steps in the diagnosis of the ocular deviation. He claimed that occlusion of the good eye served to develop the acuity, fixation and rotations of the squinting eye and made possible more accurate retinoscopy and subjective refraction. In spite of some theoretic objections to the test, Hughes [9] claimed that it is of inestimable value in cases of obscure symptoms which are believed to be of ocular origin.

Monocular occlusion has not been universally accepted. Duane and Berens,[10] for example, questioned the value of the test, insisting that it did not reveal true hyperphoria but caused an artificial dissociation of the visual planes. This was Lancaster's [11] belief. He gave up the test as a method of measuring the amount of heterophoria but continued to use it in treatment of the symptoms of heterophoria and other defects of binocular vision. He expressed the belief that a positive result (relief from symptoms following monocular occlusion) was strong proof that the patient's symptoms were due to a disturbance of binocular vision. In many cases, if relief could not be obtained by treatment of these defects, he advised the patient to continue monocular occlusion indefinitely—for example, for all near work. Lancaster stated that he was convinced, however, that failure to get relief from symptoms does not necessarily prove that binocular vision is not at fault.

Zentmayer [12] has never written on monocular occlusion. He stated, however, that he had used it to some extent in his office practice. He said he was not convinced that the monocular occlusion test is a satisfactory way of uncovering latent muscular imbalance and that he would be influenced by the result only in a case in which the usual methods had given contradictory and variable evidence.

Abraham [13] questioned the value of the test on the ground that it demonstrated Bell's phenomenon, a normal sign, in which the covered eye turns upward and outward, as in sleep or the early stages of anesthesia, so that the test could not be a method of uncovering latent heterophoria. Beisbarth [14] stated his opinion that the test was impractical, basing his objections on a series of 29 cases. He asserted that the good results claimed by some authors could be accounted for by the fact that they had not prescribed full correction for the amount of heterophoria measured after occlusion.

Marlow [15] replied to the criticisms of Abraham and Beisbarth by discounting their adverse results on the grounds of inadequate procedure, too short a period of occlusion (one to twenty-four hours only), too few cases and incomplete observations. Marlow [15] admitted that prescribing for the heterophoria is not always simple. He pointed out that the amount of the error alone was not the deciding factor, but that one's decision must be controlled, or modified, by a comparison of the fusional amplitudes, the amount of the heterophoria in different directions of gaze and the difference brought out by occlusion of the other eye.

Duke-Elder [16] spoke of binocular vision as a perceptual process of considerable complexity and divided it into two stages: First, a sensory image is elaborated simultaneously by each uniocular mechanism, and second, if the two images are suitable, they are fused into one by a perceptual process on a higher level.

Up to the present, little attention has been paid to the possibility that aniseikonia is the binocular anomaly at fault when a patient's symptoms have been partially or wholly relieved by the occlusion of one eye. Since aniseikonia (a relative difference in size and/or shape of the ocular images) is a binocular anomaly, it is reasonable to assume that persons suffering from this disturbance should be relieved of their symptoms when binocular vision is suspended. It be-

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8. Worth, C.: Worth's Squint, edited by F. B. Chavasse, ed. 7, Philadelphia, P. Blakiston's Son & Co., 1939, p. 435.

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10. Duane, A., and Berens, C., Jr.: Ocular Movements, Ophth. Lit. **17**:53, 1921.

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15. Marlow, F. W.: Recent Observations on the Prolonged Occlusion Test, Am. J. Ophth. **16**:519-527 (June) 1933.

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comes still more imperative to consider aniseikonia as the causative factor in cases of occlusion in which no latent heterophoria or any disturbance of the accommodation-convergence relationship is revealed.

PRESENT STUDY

During the past two years we have accumulated data on a series of 80 patients who had recourse to monocular occlusion. Many of these patients had resorted to closing one eye of their own accord. They had become aware of the fact that what they had regarded as a habit had gained for them relief from distressing symptoms which were present whenever they used their two eyes together. With a few of the patients monocular occlusion had been tried for diagnostic purposes by other physicians. Some of the patients were referred because their symptoms were relieved by occlusion, and other therapeutic measures had failed to help them. With a large number of the patients occlusion was resorted to when correction of the usual ocular defects had failed to give relief.

The Dartmouth Eye Institute devotes special attention to the study of eyestrain, and refractive errors are looked on as its most frequent cause. The great number of patients with problem cases who come to the Institute have repeatedly had their refractive errors measured and corrected elsewhere.

We examined the refraction of this series of patients with great care, using methods of measuring the accommodation and refraction which were far beyond those in general use. When required, examinations were made with cycloplegia, and stigmatoscopy was also employed. The final check in the more troublesome cases was made by Dr. Walter B. Lancaster, who was our chief at that time.

Of the 80 patients, 56 (or 70 per cent) obtained partial or complete relief from their chief symptoms while they had monocular occlusion. Nineteen patients reported having received no relief whatever, a few stated that their condition was worse, and 5 gave indefinite information. Of the total number, 49 were found to have a significant degree of aniseikonia, and 9 a significant amount of latent heterophoria, after the occlusion of one eye. Twenty patients had both aniseikonia and a motor anomaly. Two patients showed no binocular anomaly.

The number of patients with aniseikonia was relatively higher than the number with latent heterophoria. This is explained by the fact that a greater number of the patients were referred to the Institute primarily because aniseikonia was suspected and motility factors had been fairly well ruled out. There is no doubt that we have occasion to employ monocular occlusion more often than one would find necessary in the average ophthalmic practice. But no practice lacks that small group of patients with whom all measures have failed to give relief from their distressing and persistent symptoms. These patients constitute an important group for diagnosis and treatment.

The results obtained with our group of 80 patients are tabulated as follows:

Total no. of patients	80	(100%)
No. with binocular anomaly corrected	62	(77%)
No. relieved	44	(55%)
No. not relieved	18	(22%)
No. who continued monocular occlusion as therapeutic measure	11	(14%)
No. with indefinite or no report	7	(9%)

Our technic begins with the taking of the patient's history. Many patients, on being questioned, report that they have found they could read, watch a movie or baseball game or travel by car or train much more comfortably with one eye closed or covered. Some people speak of closing one eye habitually in bright sunlight; again, the eye of a patient has been seen to close as a reflex act, so that annoying diplopia is prevented. Such information is important in the later evaluation of the patient's binocular performance.

When monocular occlusion is decided on, its purpose should be clearly explained to the patient. He must be assured that no harm can come from his having one eye covered. The patient should be warned of the necessity of becoming accustomed to one-eyed vision and of the inability to judge distances accurately with one eye alone. It is well to caution him about going through doorways and up and down stairs, pouring liquids and setting things down, and against driving a car or working in a hazardous occupation.

Members of the staff have at different times employed monocular occlusion for several days in order to become familiar with the peculiarities of monocular vision and the changes in phoria following occlusion. It is helpful to try monocular occlusion with a few persons who have no symptoms in order to gain knowledge of the normal changes in the measurement of phoria following monocular occlusion and of the annoyance of one-eyed vision itself to persons who enjoyed comfortable binocular vision before the test. If a patient reports that his having one eye covered was a bit annoying, but not nearly as troublesome as his headaches were, one can better realize how much of a burden his headaches must have been.

There are many ways of occluding one eye. Marlow[1] used a ground glass lens or a black court plaster. If a patient does not wear glasses, gauze and cotton held in place over the eye by a black patch (figure, *A*) can be employed. This necessitates his keeping the lid closed, which is often objectionable.

There are many types of translucent lenses which prevent fusion and afford partial occlusion (figure, *B*). A flesh-colored bakelite shield (figure, *C*) made to fasten on the front of the spectacle lens is often quite satisfactory. It does not give complete occlusion, as light enters from

It is of little value to try monocular occlusion for a few hours only—in fact, even for one or two days. In order for the test to be of value, occlusion of one eye should be maintained for at least two weeks. In general, most patients are more annoyed than helped by only a few days' occlusion; relief from symptoms of binocular origin can be masked by the more or less temporary annoyances of one-eyed vision.

Measurements of the degree of heterphoria should be made immediately on removal of the occluder. One should be familiar with the range of these measurements after prolonged

Types of monocular occluders.

the sides. The large, black, soft rubber occluder (figure, *D*) provides complete occlusion and, at the same time, allows the occluded eye to remain open. It is, however, warm and conspicuous to wear. The best type of occluder[17] that we have used is one which is attached by suction to the back of the lens and fits around the orbit (figure, *E*). It is relatively inconspicuous and is light in weight. It permits the eye behind it to remain open and cuts out most of the light from the sides. The most inconspicuous occluder possible is an opaque contact glass (figure, *F*), with which some of our greatest successes, from a therapeutic standpoint, have been obtained.

occlusion of one eye, since it is known that a covered eye tends to turn upward and outward. Whenever a hyperphoria is measured after the occlusion of one eye one should occlude the other eye for a similar period and repeat the tests. An alternating hyperphoria, termed dissociated vertical divergence by Bielschowsky,[18] is often met with when occlusion is carried out on the other eye. This is a purely innervational type of deviation and is not amenable to correction by either prisms or surgical means. We have repeatedly observed that the vertical fu-

17. The Watchemoket Optical Company's "Vac Cluder."

18. Bielschowsky, A.: Lectures on Motor Anomalies of the Eyes: Physiologic Introduction, Arch. Ophth. **12**:805-818 (Dec.) 1934.

sional amplitudes in cases of dissociated vertical divergence are higher than normal and may be equal.

The amount of lateral heterophoria measured after occlusion offers no new problem. One deals with it in the usual manner. Frequently, there is more exophoria (or less esophoria) after occlusion. The amount of error alone cannot be the deciding factor in the prescription for heterophoria after occlusion. The fusional amplitudes, for both distant and near vision, with the measurements repeated, after the occlusion of the other eye, must all be taken into consideration before the final prescription or the treatment of any latent heterophoria is decided on.

At the Dartmouth Eye Institute monocular occlusion is not employed solely as a means of uncovering latent heterophoria but is used as a test to determine whether a binocular anomaly may be causing the patient's trouble. If a patient has found relief from his chief symptoms during the occlusion test, consideration is given not only to factors previously considered by others who tried occlusion but to the binocular anomaly of aniseikonia. The important information to be gained from the occlusion test, it is believed, concerns whether there is any relief from symptoms. A negative report is not conclusive evidence that no binocular trouble is present. The patient himself can decide whether his annoyance with monocular vision was greater or less than that, for instance, which he had experienced from his headaches. His report made after occlusion must be carefully weighed against statements before occlusion was tried. A patient may complain at great length of his discomfort while he wore the occluder, but only on his being questioned will he admit that he had no headache after the first three or four days. In general, patients who have suffered for years will gladly submit to the occlusion test. If they obtain only partial relief from their symptoms, they feel encouraged and will follow the treatment and advice with renewed hope.

A high percentage of our patients were given relief by correction of their binocular anomaly. A few could not be given comfortable binocular vision but were later provided with comfortable monocular vision. Dr. Walter B. Lancaster devised a treatment for 2 such patients by prescribing an opaque contact glass, with an iris painted on the glass to match that of the other eye. In 1 of these patients, a young woman, a lesion developed in the fovea of one eye from exposure to very bright light while she was polishing a concave telescopic mirror. The second patient had constantly fluctuating heterophoria and obtained complete relief with an opaque contact glass. A third patient had had a successful operation for detachment of the retina but could not obtain binocular vision in the area of binocular fixation because of macular micropsia, although there was good fusion in his peripheral fields. He adopted permanent occlusion willingly in order to avoid the confusion caused by the overlapping of small objects centrally fixated.

Eight other patients in our series have resorted to some form of monocular occlusion in order to be comfortable. Interesting data are set forth in the following tabulation:

Total number of patients............	80	(100%)
Patients relieved during occlusion....	56	
No. of these relieved by treatment...	47	(59%)
Patients not relieved during occlusion	19	
No. of these not relieved by treatment.	13	(16%)
No. of these relieved by treatment...	5	(6%)
Patients with indefinite results with regard both to test and to treatment..	11	(14%)
Patients with relief during occlusion but not with treatment............	4	(5%)

Fifty-six patients in the entire series were given some relief during occlusion. Of these, 47 obtained relief through correction of their binocular anomalies, which were revealed by the occlusion test. This is evidence of the positive value of the occlusion test. This series of patients stood an 8:10 chance of obtaining ocular comfort by correction of heterophoria or aniseikonia or a combination of the two anomalies. Five of the 19 patients who reported that they had no relief during occlusion obtained ocular comfort when their binocular difficulties were treated. These patients stood a 1:4 chance of obtaining relief by correction of their binocular difficulties, although the occlusion test gave negative results.

SUMMARY AND CONCLUSIONS

Comfortable binocular vision is frequently not obtained because the anomalies of binocular vision have not been taken into consideration.

While monocular occlusion is generally employed for the purpose of discovering latent heterophoria, we advocate it as a means of determining whether any of the various binocular anomalies are at fault.

In the series of patients reported on for whom monocular occlusion was employed, consideration was given not only to latent heterophoria but to disturbances of the accommodation-convergence relationship and to aniseikonia.

Dartmouth Eye Institute.

CATGUT SUTURES FOR CLOSURE OF THE DEEP CORNEOSCLERAL WOUND IN OPERATIONS FOR CATARACT

A PRELIMINARY REPORT

FREDERICK ALLISON DAVIS, M.D.
MADISON, WIS.

The growing popularity of some form of ıture of the so-called deep corneoscleral wound ı operations for cataract has led me to try most : the types of sutures recommended by various ırgeons. Difficulties have been encountered in ısertion of many of these sutures while some, ı my opinion, produce an unsatisfactory closure f the wound. For this reason I have recently ·ied various types of catgut. With the use of atgut one may insert one or more sutures in ıe deep wound and completely cover the wound ith a conjunctival flap, the latter being sutured eparately with silk.

METHOD

I prefer to make the usual limbal section with a on Graefe knife, with a complete conjunctival flap overing the entire deep corneoscleral wound. This an be most easily accomplished if the conjunctiva is ushed down with a spatula, or other semisharp instrument, before the section is begun, which frees it at the mbal borders.

The point of the knife is first inserted beneath the onjunctiva about 2 mm. from the limbal border, at ıe site chosen for the section, and advanced to the mbus, and the corneoscleral incision is begun in the sual manner. After the counterpuncture a similar lip f conjunctiva is obtained and the section completed, ıe incision being carried deep enough to permit a omplete conjunctival flap throughout.

After the section, depression of the knife usually aids ı securing a flap of the desired size. Also, one may btain a slight scleral lip at 12 o'clock. After the ection one plain five 0 catgut suture, fitted in a fine eedle with a cutting edge, is immediately inserted and ıe loop drawn aside. To insert the suture, the corneal p of the wound is grasped with forceps, and the needle ; inserted through the outer third of the margin of ·ound, after which the needle is similarly inserted nmediately opposite in the outer, or scleral, lip of the ·ound. When the suture is tied, perfect apposition of ıe lips of the wound is obtained. At times I have sed two or more catgut sutures, especially if the coreal side of the wound could be easily grasped. At ıe end of the operation the conjunctival incision is losed with six or more silk sutures. Two of these an be inserted before delivery of the lens if one is pprehensive. The cataract is then removed in the ıanner desired and the catgut suture immediately tied ·ith two or three knots.

The insertion of the needle into the corneoscleral ·ound is not easy and requires great delicacy and care in manipulation to avoid undue trauma to the globe. If one uses the keratome-scissors technic in opening the globe, the suture is more easily inserted. When employing this technic, I usually dissect an ample conjunctival flap 4 mm. wide at its highest point and tapering to the sides. The keratome can be so introduced that one is certain of obtaining a good scleral lip on the corneal border of the incision for insertion of the suture. The needle is more easily inserted before the wing sections are completed with the scissors.

COMMENT

My series of operations, while considerable, is not yet large enough to justify one's drawing any final conclusions concerning the efficacy of the buried catgut suture, but so far its use has proved entirely satisfactory. The lips of the deep wound have remained in perfect apposition, with no spreading or separation. The conjunctiva has shown no bulging or elevation over the suture, and the reaction has been no greater than that which is generally encountered after the same procedure without the deep suture.

Most of the patients could have been discharged from the hospital on the tenth or twelfth day. In 1 case the patient refused to permit the use of a patch on the eye which was not operated on. The operative wound healed perfectly, with almost no reaction, and the patient was ready for discharge on the twelfth postoperative day in spite of this unusual practice.

The plain catgut disappears completely and usually cannot be identified at the end of a week. Chromic catgut requires a much longer period for complete absorption. In a case in which a five 0 chromic catgut suture was used and tied with three knots the catgut absorbed slowly, and at the end of two weeks part of the knot eroded through the conjunctiva. However, this in no way interfered with prompt and firm closure of the deep wound. Plain catgut is more pliable and absorbs much more quickly and completely, and therefore should be preferred. It has so far proved more satisfactory than the chromic gut, for the reason indicated.

Finer catgut, that is, six 0 or seven 0, would be preferable, but so far I have been unable to obtain it.

From the Department of Ophthalmology, University of Wisconsin Medical School.

The use of buried catgut sutures affords the surgeon the opportunity to make the section unhampered by preplaced sutures, or partial incisions, which, in my opinion, interfere with, and at times mar, the beauty and precision of the free von Graefe incision.

Since I introduced the use of buried catgut sutures in operations for strabismus, in 1934,[1] my associates and I employed buried catgut sutures in more than 500 operations for strabismus, without a single deep infection. Superficial conjunctival sutures slough out or break down at times, but in no instance that I can recall has the deep suture become loosened or infected. Occasionally a conjunctival cyst has developed, possibly as a result of irritation from the buried chromic catgut, but such a complication has been rare. In cases of operation for strabismus swelling over the site of the sutures in both the recession and the resection procedure sometimes occurs and may last for some time. This has not yet occurred in my cases of cataract extraction. I am at present trying various types of needles, but I find an atraumatic needle supplied by Davis & Geck, Inc., the most satisfactory.

A more complete report will be made when a larger series of operations has been completed and the final results are evaluated.

Note.—Since this article was submitted for publication, my associates and I have used buried catgut sutures in more than 70 extractions. No unusual complications have been encountered, although postoperative hyphemia has been observed in a few cases. Slight swelling beneath the conjunctival flap developed in some instances, apparently due to edema incident to the liquefaction and absorption of the catgut. This usually absorbs completely by the end of the fourteenth day or sooner. No undue irritation seems to accompany this slight swelling, nor has the conjunctival flap failed to flatten out with its disappearance. As already stated, however, in most cases there is little visible evidence of the suture aside from a small light spot at the site of the knot.

The deep corneoscleral wound has been observed to be firmly closed, without exception, at the time of the first dressing, usually on the fourth postoperative day, with full restoration of the chamber. No subsequent spreading of the wound has been seen; so it is assumed that the swelling of the flap occasionally encountered is incident to the presence of the catgut. However, it is completely absent in most cases. I have not yet been able to determine why the swelling is present in some cases and is absent in others.

We are now using plain catgut exclusively in cases in which this technic is employed, since it unquestionably absorbs more quickly and seems to hold the wound sufficiently tight to permit firm closure before absorption takes place. The suture is tied firmly with two knots, and the ends are cut short in order to reduce the amount of gut for absorption.

It is surprising how little irritation accompanies the presence of the catgut. The eye shows no more reaction than is usually seen with cataract extractions. Occasionally injected blood vessels in the flap may persist for a short time, but deep inflammation of the globe or severe iritis has not so far been encountered.

The suture seems to be safe; it is relatively simple to introduce as compared with many other kinds, and to surgeons who are advocates of the conjunctival flap it offers the advantage of a complete covering of the deep wound, which, in my opinion, is highly desirable.

224 West Washington Avenue.

1. Davis, F. A.: Modification of Jameson Recession Operation for Strabismus, Arch. Ophth. **11**:684-687 (April) 1934.

TWO PLASTIC OPERATIONS FOR REPAIR OF ORBIT FOLLOWING SEVERE TRAUMA AND EXTENSIVE COMMINUTED FRACTURE

JOHN MARQUIS CONVERSE, M.D.
NEW YORK

War injuries of the middle third of the face may result from head-on crashes in motor and aviation accidents and from the unpredictable ravages of bullets or bomb fragments.

In crash accidents, when the head is thrown straight forward, severe comminution of the bones of the "interorbital region" (nasal pyramid, lacrimal and ethmoid bones) may result. Comminution and posterior displacement may produce considerable overriding of the fragments, as well as displacement of the internal palpebral ligament, resulting in a marked deformity (fig. 1 *A*). If the head is thrown forward while turned laterally, the malar region may present multiple fractures, with resultant displacement of the floor of the orbit into the antrum (fig. 5 *A*). It is evident that immediate replacement of the displaced bones is the method of choice. New methods of early treatment of such injuries have been described elsewhere.[1]

Two cases are presented to illustrate methods of late reconstruction.

CASE 1.—*Reconstruction following disorganization of the medial wall of the orbit and the nasal bones by a bomb fragment.*

W. L, a man aged 23, was wounded in an air raid on May 8, 1941, when a bomb struck his home, killing all the other members of his family. A fragment of the bomb entered the left preauricular region, penetrating the orbit and the nasal cavity and making its exit through the right lateral aspect of the external nose. Six months later the patient was seen for repair of a saddle nose, due to destruction of the cartilaginous support, of most of the nasal lining and of the nasal bones. The remains of the left nasal bone and of the ascending process of the maxilla on the left side appeared to have been pushed into the ethmoid sinus (fig. 2 *A*). The whole region of the inner canthus of the left eye was widened (fig. 2 *B*). The eyeball seemed to have been pushed laterally (fig. 1 *A*). Vision was lost in the left eye, as a result of section of the optic nerve. Plastic repair was planned in two stages: (1) correction of the deformity of the inner canthus and (2) repair of the nasal deformity.

Operation (Feb. 15, 1942).—With local anesthesia, induced with a 1 per cent solution of procaine hydrochloride to which had been added epinephrine hydrochloride (10 drops of a 1: 1,000 dilution to each 100 cc. of anesthetic), which was allowed to infiltrate along the medial wall of the left orbit, an incision about 5 cm. in length was made, starting laterally and extending to the medial end of the eyebrow (fig. 3). Subperiosteal elevation of the tissues was done with a small elevator; the disinserted internal palpebral ligament was defined; the scarred remains of the lacrimal sac was visualized, and, with the dissection continued back over the overriding osseous fragments, the os planum of the ethmoid bone and the anterior ethmoidal artery and nerve were exposed. The protruding bone was resected with a fine osteotome and a rongeur (fig. 3) until the bony wall appeared to be on the same plane as the os planum farther back The remains of the sac were removed, as there was not enough of the sac left to permit a

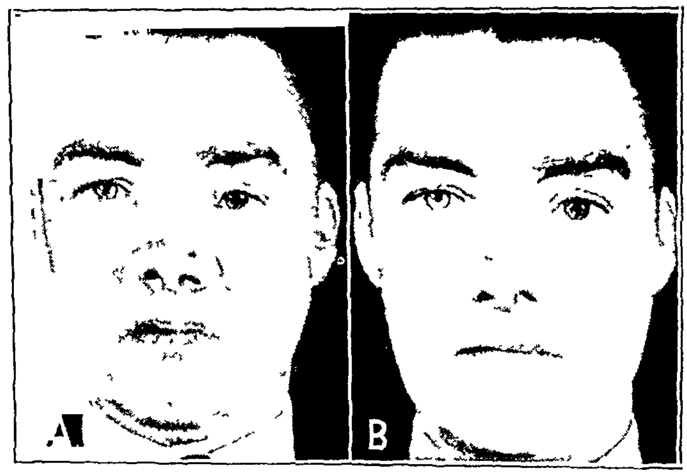


Fig. 1.—*A*, appearance before replacement of the medial canthus; *B*, appearance after replacement of the medial canthus and reconstruction of the nose.

Toti-Mosher operation. The inner canthus of the left eye tended to resume its normal place. The internal palpebral ligament was then sutured to remains of periosteum with a gage 35 stainless steel wire (fig. 4). (The ligament could also be sutured to the bone by looping the wire through two small holes drilled in the bone without perforation of the nasal mucosa.) The cutaneous incision was then carefully sutured with fine interrupted silk sutures.

The result of the operation eliminated the unilateral mongoloid appearance. The nasal deformity was later repaired (fig. 1 *B*). The type of operation performed in this case should be valuable in all cases in which traumatic splaying of the nasal bones or telescoping of the bones into the ethmoid cells has produced widening of the intercanthal distance.

From the American Hospital in Britain and Churchill Hospital, Oxford, England (1940-1942).

1. Converse, J. H.: Some Aspects of Emergency Plastic Surgery in War Injuries of the Face, Ann. Otol., Rhin. & Laryng. **52**:637 (Sept.) 1943.

CASE 2.—*Reconstruction of the floor of the orbit after comminution, with downward displacement of the eyeball.*

W. G., aged 21, a private in the British army, received severe injuries to the head on Feb. 24, 1942, sustained by his striking a large rock on the roadside when he leaned his head out of an army truck which was traveling at high speed. He was treated in an emergency hospital for multiple lacerations of the face, fracture of the mandible and maxilla and comminuted fracture of the malar bone, with depression into the antrum. At this emergency hospital the fractures of the jaw were treated and the lacerations sutured, but no attention was given to the fractured malar bone. Three months later I saw the patient; at this time plastic repair of the floor of the orbit was under consideration because of persistent diplopia. Movements of the extraocular muscles were normal. The left eyeball appeared lower than the right; comparative measurements showed that the floor of the left orbit was 18 mm. lower than the floor of the right orbit (fig. 5 *A*). Diplopia was constant and necessitated his wearing a patch over the left eye.

Operation (June 16, 1942).—With the use of spinal anesthesia induced with procaine hydrochloride, an incision, 12 cm. in length, was made over the crest of the right ilium posterior to the anterior superior spine. The periosteum was incised and elevated, together with the muscular attachments to the crest. The inner table was exposed by elevation of the iliac muscle. With the aid of osteotomes, a piece of bone 5 by 4 by 3 cm. was removed from the inner table of the ilium. The wound was then closed, plane by plane, with interrupted silk sutures.

With local anesthesia and infraorbital block induced with a 1 per cent solution of procaine hydrochloride containing epinephrine hydrochloride, an incision was carried along the whole length of the lower lid, in one of the cutaneous folds; the orbicularis muscle fibers were split, and the periosteum along the lower border of the orbit was incised and elevated along the entire length of the floor (fig. 6). A calibrated, double-bladed instrument was then introduced and used to elevate the eyeball. The patient's diplopia was then tested, but his answers were contradictory. The bone graft was shaped with the aid of the Albee electric saw and fitted into position, the eyeball being elevated 18 mm. The periosteum and the orbicularis muscle were then sutured with fine catgut, and the skin was closed with fine interrupted silk sutures. A drop of atropine solution and boric ointment were instilled in the eye. A pressure dressing was used and was

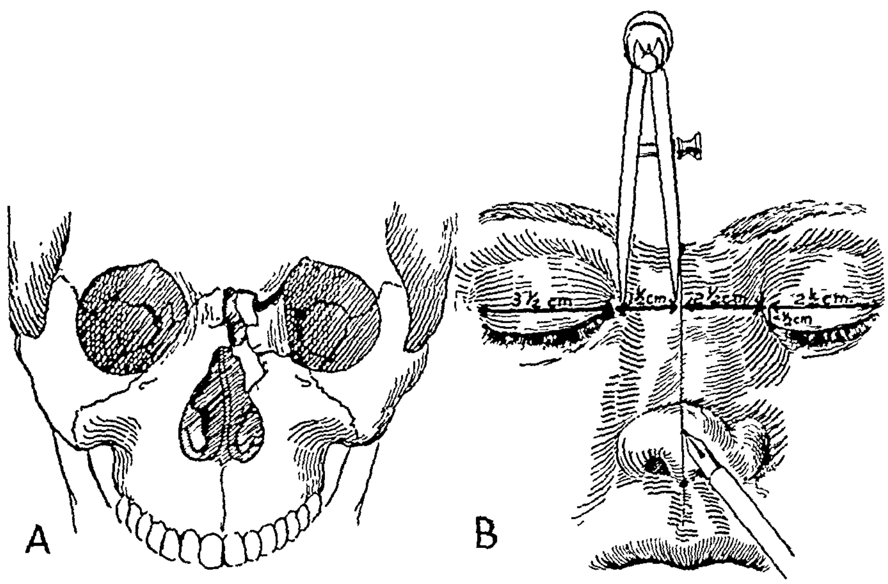


Fig. 2.—*A,* diagrammatic representation of displacement of bone, which penetrates the orbital cavity; *B,* measurement of lateral displacement of the left medial canthus.

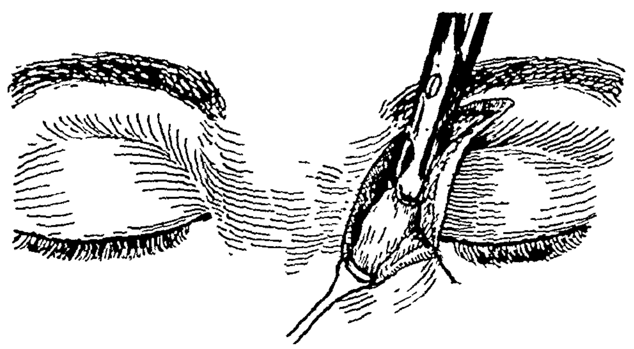


Fig. 3.—Drawing showing removal of a fragment of bone which is projecting into the orbit.

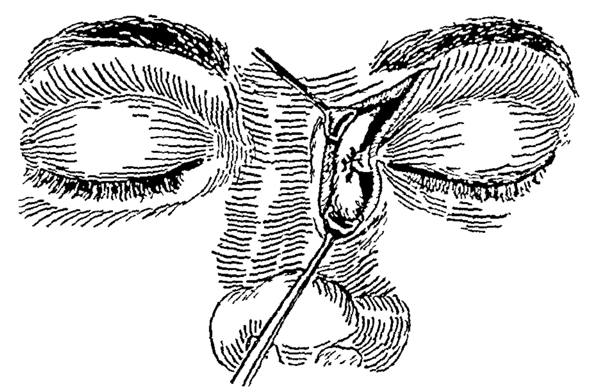


Fig. 4.—Suture of the internal palpebral ligament into the periosteum.

left undisturbed for five days. Two weeks after the operation the diplopia had disappeared except in extreme upward gaze. The patient's appearance was considerably improved (fig. 5 *B*). (A small rotation flap corrected the ectropion.)

COMMENT

This procedure is not new. Cartilage (costal) has been used to elevate the eye.[2] The inconvenience of cartilage, however, is its tendency to curl, which renders its use less precise than

Fig. 5.—*A*, ptosis of the floor of the orbit, with diplopia; *B*, after elevation of the orbital floor by a graft from the ilium.

that of bone. Bone grafts from the ilium have been employed in the orbit by Gillies, in England. Bone grafts have also been used in the repair of noses and defects in the skull and as contour material around the face. There is clinical evidence of their reossification and survival when they are placed subperiosteally, against bone. Wheeler[3] advised the use of fascia lata, but this has the disadvantage of not being sufficiently solid and firm to bring about a suitable elevation. The present tendency toward the use of acrylics as buried material might well find an application in the reconstruction of the floor of the orbit, either as a temporary support, before the introduction of bone, or as a permanent means of reconstruction.

DISCUSSION

DR. R. TOWNLEY PATON, New York: Dr. Converse has made a valuable suggestion in the use of stainless steel wire to reattach the internal palpebral ligament. Often the periosteum has been destroyed in this region, so that a poor cosmetic result is obtanied in an attempt at reattachment.

His most valuable suggestion is the method described for elevation of an eye after fracture of the floor of the orbit; this may be applied after enucleation in cases in which there is downward displacement of the prosthesis. The cosmetic result obtained after the removal of old phthisical eyes is often discouraging, the poor effect being due to sagging of Tenon's capsule and loss of elasticity of the tissues in and about the orbit. Ptosis of the lower lid frequently accentuates the condition, and there may be slight ectropion as a further complication. It has been my experience that a modified Kuhnt-Szymanowski operation, for repair of ectropion, is not sufficient to draw the artificial eye upward, even when both cul-de-sacs are large and roomy. A disfiguring narrowing of the palpebral fissure may result from this method of treatment, whereas the operation described by Dr. Converse, which employs a bone-shaped wedge, is especially applicable. The only difference is that the implant in Tenon's capsule is elevated, and not the eyeball, as in the case just described. It is a confession of weakness on the ophthalmologist's part that he does not use bone implants more frequently and that fat and cartilage are used as substitutes. In 2 cases a good cosmetic result was obtained by removal of the gold ball implant and its reinsertion in Tenon's capsule after a

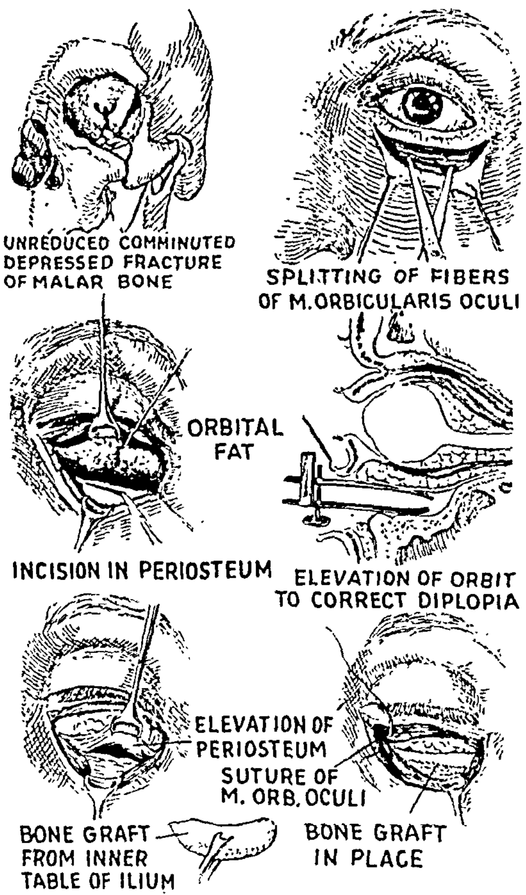


Fig. 6.—Drawings (D. Stilwell) illustrating steps in elevation of the floor of the orbit with a bone graft.

tuck was taken in the lower surface of the capsule. This method is not to be recommended, however, as it may lead to serious impairment of the function of the ocular muscles. The use of vitallium wedges for this purpose will be discussed later.

927 Park Avenue.

2. Spaeth, E. B.: The Principles and Practice of Ophthalmic Surgery, Philadelphia, Lea & Febiger, 1939, pp. 74-76.

3. Wheeler, J. M.: Operative Replacement of Dislocated Inner Canthus and Depressed Outer Canthus: Filling of Sunken Orbit with Fascia Lata, in Collected Papers of John M. Wheeler on Ophthalmic Subjects, New York, Columbia University Press, 1939, pp. 425-429.

PRACTICABILITY OF USE OF CONTACT LENSES AT LOW ATMOSPHERIC PRESSURES

CHARLES E. JAECKLE, M.D.

SOUTH ORANGE, N. J.

Present standards for personnel of military planes require that crew members have good vision without glasses. The use of ordinary spectacles is considered impractical. Since many persons otherwise qualified are excluded from this branch of the service, in a time of great need, by reason of ametropia, the question may be fairly asked, "Can contact lenses be used practicably in planes at the altitudes commonly attained in modern warfare?" The observations here reported were made in an attempt to answer this question.

Numerous studies of ocular function have been made under conditions of low atmospheric pressure, and hence low partial pressure of oxygen. These studies were reviewed by McFarland, Evans and Halperin.[1] In modern flying, plane personnel need not experience lack of oxygen, since oxygen may be supplied by means of a mask. A normal supply of oxygen to the cornea via the blood stream and the intraocular fluid may therefore be maintained. When only the mouth and nose are included in the mask, however, the cornea is exposed to an atmosphere of low oxygen pressure. Since oxygen diffuses directly from the atmosphere to the cornea, this fact should be kept in mind.

PRESENT STUDY

Material.—In the present experiment, the temperature was kept constant at within 3 degrees of 73 F.; the atmospheric pressure was varied, and the partial pressure of oxygen was maintained by use of oxygen masks when the atmospheric pressure fell below that comparable to an elevation of 10,000 feet (about 3,000 meters).

Eleven observations were made in a pressure chamber on both eyes of 10 volunteer subjects[2] who were accustomed to using contact lenses. Two of the subjects were females and 8 were males. The ages of 9 subjects ranged from 17 to 33 years; 1, a woman, was 56 years old. One subject had used contact lenses only 2 months; 4 had used them five months; 3, ten to fourteen months, and 2, two years or longer. One could use them with comfort and clear vision for one and a half hours; 2 for three and a half to four hours; 1, for five hours, and 6, for seven to ten hours. One had keratoconus and 2 aphakia. Only 1 subject admitted having noted bubbles under the lens after it was inserted.

Procedure.—Each subject used the solution to which he was accustomed. Each inserted the contact lenses from one half to one hour before the experiment was begun.

Visual acuity was determined by the Snellen chart. The conjunctiva was examined grossly. The fit of the contact lens was noted. The cornea was examined with the slit lamp without removal of the lens. (The lens was removed from one eye in examination of the first 2 subjects; the manipulation of getting the lens out and in again, however, was followed by some conjunctival injection, and it was thought that this might obscure possible subsequent changes.)

The subject and the observer then entered a pressure chamber equipped with a Snellen chart at a distance of 10 feet (3 meters) and with oxygen masks. The atmospheric pressure in the chamber was lowered.[3] The temperature was kept constant. Observations were made at various levels of pressure, the visual acuity and the gross appearance of the conjunctiva, the cornea, the contact lens and the fluid being noted. The subject was not permitted to look at the chart between observations, and various devices, such as having him name the letters in irregular order, were employed to discourage his memorizing the chart. The subject was asked to report any discomfort or blurring of vision. Each "flight" lasted about one hour. At the end of this period, visual acuity was again taken with the Snellen chart, with the subject outside the chamber, and the conjunctiva and cornea were examined with the slit lamp, with the use of fluorescein.

OBSERVATIONS

Observations were made on 22 eyes. The visual acuity of 12 eyes was 10/10 or better; that of 8 eyes, 10/15 to 10/20, and that of 2 eyes, 10/25. In only 1 eye (subject 9) did visual acuity change by more than two or three letters, a variation which is not considered significant. The acuities are, therefore, given only for subject 9.

From the Department of Ophthalmology, Northwestern University Medical School.

This study was undertaken at the request of the Subcommittee on Ophthalmology of the National Research Council.

1. McFarland, R. A.; Evans, J. N., and Halperin, M. H.: Ophthalmic Aspects of Acute Oxygen Deficiency, Arch. Ophth. **26**:886 (Nov.) 1941.

2. The late Dr. Sanford R. Gifford and Dr. Theodore Zekman referred the subjects for study, and Dr. Gifford gave advice in the investigation.

3. Dr. A. C. Ivy, head of the department of physiology, Northwestern University Medical School, gave the use of the pressure chamber, and Dr. Harry F. Adler, of the same department, operated the chamber and offered valuable suggestions in the course of the experiment.

SUBJECT 1.—A man aged 29 had used contact lenses six months. He saw halos after three and a half to four hours.

The minimal pressure was equivalent to that at an elevation of 10,000 feet (about 3,000 meters), attained in thirty minutes. Ten minutes later the subject reported that the eyes felt irritated but that vision was sharper. After the pressure was held thirteen minutes at a level equivalent to that at an elevation of 10,000 feet, it was reduced. No changes were observed in visual acuity, in the appearance of the cornea or conjunctiva or in the fluid in the contact lens.

SUBJECT 2.—A woman aged 56, with aphakia, had used contact lenses over two years; she experienced diminishing vision after wearing them from five to six hours.

A minimal pressure equivalent to that at an elevation of 10,000 feet (about 3,000 meters) was attained in thirty minutes; the "descent" was made at the end of ten minutes. No subjective irritation or change in vision was observed. There was no change in visual acuity, and the cornea, the conjunctiva and the fluid in the contact lens showed no alteration.

SUBJECT 3.—A man aged 29, an Army officer, had used contact lenses six months. He experienced discomfort after wearing them eight hours.

A maximum "elevation" of 10,000 feet (about 3,000 meters) was attained in twenty-five minutes. The subject reported that his vision was better. Ten minutes later he noted "irritation." No change was observed in visual acuity, in the appearance of the cornea or conjunctiva or in the fluid in the contact lens.

SUBJECT 4.—A man aged 33, a business man, made frequent trips by plane; he had used contact lenses for fourteen months, with comfort for periods of ten hours. He had never experienced discomfort or blurring during commercial flights.

A maximum "elevation" of 10,000 feet (about 3,000 meters) was attained in twenty minutes. He reported that his vision was sharper. No change was noted in visual acuity or in the cornea, the conjunctiva or the fluid in the contact lens.

SUBJECT 5.—A man aged 20 had used contact lenses ten months. He stated that he saw halos after wearing the lenses three and a half hours and that occasionally a small bubble formed after the lens had been inserted and worn a while. This may have been evidence of a poor fit. There was a small bubble under the left lens, over the upper part of the cornea, at the start of the "flight."

A pressure equivalent to an elevation of 10,000 feet was attained in nineteen minutes, without changes. Seven minutes later, at a pressure equivalent to an elevation of 18,000 feet (about 5,500 meters), two small bubbles appeared over the upper part of the right cornea and a large and a small bubble over the upper part of the left cornea. At the beginning of the "descent," nine minutes later, the bubbles over the right eye had coalesced, and those over the left eye had not changed. At an "elevation" of 10,000 feet (about 3,000 meters), ten minutes after the "descent" was begun, the bubble on the right side was slightly smaller; the bubbles on the left side were unchanged, and a larger bubble was seen at 2 o'clock on the scleral rim. All the bubbles became smaller as the decrease in pressure continued. No change in visual acuity or in the appearance of the cornea or the conjunctiva was noted.

SUBJECT 6.—A man aged 30 had used contact lenses for five months; he experienced halos and tearing after wearing them one and a half hours. He had never had bubbles under the lens. A pressure equivalent to that at an elevation of 10,000 feet was attained in seven minutes, without changes. A maximum "elevation" of 18,000 feet (about 5,500 meters) was attained in fifteen minutes. A small bubble appeared over the upper part of the right cornea and remained for ten minutes (at a pressure equivalent to that at an elevation of 18,000 feet) and for an additional twenty-five minutes during the "descent" to 7,000 feet (about 2,000 meters), when the bubble appeared smaller. The bubble had disappeared by the time the ground level pressure was reached, at the end of another fifteen minutes. No changes were noted in visual acuity or in the appearance of the cornea or the conjunctiva.

SUBJECT 7.—A man aged 23, with bilateral keratoconus, had used contact lenses six years; he wore them seven hours with comfort.

A minimal pressure equivalent to that at an elevation of 20,000 feet (about 6,000 meters) was attained in twelve minutes. The decrease in pressure was begun in twelve minutes. No bubbles were noted under the lens, and there was no change in the cornea or the conjunctiva.

SUBJECT 8.—A woman aged 28 had used contact lenses eleven months. She wore them with comfort and clear vision for five or six hours, without development of bubbles.

A maximum "elevation" of 20,000 feet (about 6,000 meters) was attained in twenty-five minutes. No change in visual acuity or in the cornea or conjunctiva was noted, and no bubbles appeared in the fluid of the contact lens.

SUBJECT 9.—A man aged 22, with aphakia, had used contact lenses six months. He wore the lenses four hours with comfort, then changed the fluid and reinserted the lens, this process being repeated every four hours. Bubbles did not develop. Visual acuity with the contact lens was 10/15 in the right eye and 10/20 in the left eye at the start of the "flight."

At a pressure equivalent to that at an elevation of 25,000 feet (about 7,500 meters), which was reached in twenty minutes, visual acuity was 10/20 in both eyes. A pressure equivalent to that at an elevation of 30,000 feet (about 9,000 meters) was reached five minutes later. Several bubbles appeared over the left pupil only after the pressure had remained fifteen minutes at the 30,000 foot level. Although there was no demonstrable decrease in visual acuity, the subject saw a blur before the left eye. The bubbles did not disappear despite a slow decrease in pressure and a pause at the 20,000 foot (about the 6,000 meter) level. No change was noted in the cornea or the conjunctiva.

SUBJECT 10.—A youth aged 17, who had recently been rejected by the Air Corps, obtained contact lenses two months before coming under observation, with the hope of being admitted to this service. He wore contact lenses comfortably and with good vision seven to eight hours a day, and bubbles did not develop.

A pressure equivalent to that at an elevation of 20,000 feet (about 6,000 meters) was attained in fifteen minutes. There were six minute bubbles in a cluster over the upper part of each cornea. At 25,000 feet (about 7,500 meters), five minutes later, seven or eight small bubbles were noted over the upper portion of the right cornea and nine bubbles over the upper half of the left cornea. Visual acuity was 10/10 (no letters smaller than "10 foot size" were available). Bubbles became more numerous in the next fifteen minutes, at an "elevation" of 30,000 feet (about 9,000 meters),

and extended over the pupillary area. After the "descent" to a pressure equal to that at 20,000 feet (about 6,000 meters) in five minutes, at which level it remained for five minutes, the bubbles did not disappear. Five minutes after the ground level pressure was reached, one small bubble remained under the left lens.

The subject stated voluntarily: "The bubbles obscured vision; I could move them by blinking but if I had to shoot I'd probably miss—I could not take the time."

SUBJECT 7.—At a pressure equivalent to that at an elevation between 20,000 and 25,000 feet (about 6,000 and 7,500 meters), which was reached *in twenty minutes*, bubbles developed over the upper part of the right cornea. The pressure was increased to the 30,000 foot level and held there *fifteen minutes*. No bubbles developed under the left lens. The bubbles under the right lens showed no change after the subject had remained at the 20,000 foot level for five minutes, during the "descent." The bubbles did not enter the pupillary area and were not noticed in any way. One bubble remained ten minutes after the ground level pressure was reached. There was no change in the visual acuity or in the appearance of the cornea or conjunctiva.

SUMMARY

1. Four persons subjected to a pressure equivalent to that at an elevation of 10,000 feet (about 3,000 meters) showed no signs or symptoms.

2. Of 4 subjects subjected to a pressure equivalent to that at an elevation of 18,000 to 20,000 feet (about 5,400 to 6,000 meters), 2 had bubbles under the lenses, 1 in one eye and the other in both eyes.

3. Of 3 subjects subjected to a pressure equivalent to that at 30,000 feet (about 9,000 meters), 2 had bubbles under one lens. The third subject had bubbles under both lenses, 1 at the 20,000 and the other at the 25,000 foot (6,000 and 7,500 meter) level.

4. Of 6 persons[4] who were subjected to a pressure equivalent to that at an elevation of 18,000 feet (about 5,400 meters) or over, 5 had bubbles under at least one lens.

5. The presence of bubbles was not always associated with demonstrably lowered visual acuity. (This may have been due to the limitations placed on the method of determination of the visual acuity by the small chamber.) The subject was sometimes aware of clouding of vision, even though he might read as many letters on the Snellen chart as before the flight.

6. One of the subjects who had bubbles under the lens at high pressures could wear his lenses during ordinary activities only one and a half hours; 2 subjects wore them three and a half to four hours, and 2 subjects wore them seven to eight hours. One subject, who wore contact lenses five to six hours, had no signs or symptoms at a pressure equivalent to that at 20,000 feet (about 6,000 meters). Another subject, who wore the lenses seven hours, did not have bubbles at the 20,000 foot level in his first "flight," but had them at the 25,000 foot (6,000 meter) level in his second "flight."

7. No change in the cornea or the conjunctiva was observed.

CONCLUSIONS

The length of time the contact lenses can be worn (which may be a criterion of a good fit) was not shown to be related to the formation of bubbles.

Although the number of subjects was small, the results were rather consistent. Habitual wearers of contact lenses when subjected to pressures equivalent to those at elevations of 18,000 feet (5,400 meters) or above may be expected to have bubbles under the lenses, which will, in all probability, cause diminution of vision. This is not to be construed as a contraindication to the use of contact lenses at ordinary altitudes.

121 Irvington Avenue.

4. Subject 7 was in both the 18,000 to 20,000 foot (5,400 to 6,000 meter) and the 30,000 foot (9,000 meter) group.

STAPHYLOCOCCIC THROMBOPHLEBITIS OF THE CAVERNOUS SINUS

REPORT OF A CASE, WITH RECOVERY WITH CHEMOTHERAPY AND HEPARIN

DAVID EDELSON, M.D.
NEPTUNE, N. J.

Prior to the use of sulfanilamide and its derivatives, infectious thrombosis of the cavernous sinus was usually fatal. MacNeal, Frisbee and Blevins[1] recently collected 58 cases in which the patients recovered. In 17 of these cases the thrombosis was of staphylococcic origin. In 4 cases recovery followed expectant treatment; in 2 cases, prophylactic surgical measures; in 1 case, early radical operation; in 4 cases, bacteriophage therapy, and in 1 case, the use of antitoxin, while in the remaining 5 cases cure was obtained with various sulfonamide compounds. In a later report[2] the same authors published the results in 45 cases of thrombosis of the cavernous sinus of staphylococcic origin in which only bacteriophage therapy was given. In 14 cases the patients survived; in 23 cases they died within five days, and in 8 cases they died after a prolonged illness.

In 1941 Schall[3] reported 3 cases in which treatment with sulfonamide compounds and heparin was successful. He used sulfapyridine, sulfathiazole and 225,000 units of heparin in his first case, the first two drugs and 580,000 units of heparin in his second case and sulfathiazole and 130,000 units of heparin in his third case, 1,000 units of the heparin solution being equivalent to 10 mg. of heparin. He stated that sulfadiazine might prove later to be the drug of choice in similar cases.

Also, Ershler and Blaisdell[4] reported a case in which recovery followed the use of 106 Gm. of sulfathiazole and 129,500 units of heparin. This case was complicated by massive hematuria, so that ten transfusions (3,250 cc. of whole blood) were required to offset the severe secondary anemia which developed. The hematuria was attributed to the heparin because as soon as its use was discontinued the hematuria ceased.

Because the use of sulfonamide compounds has notably reduced the death rate from severe staphylococcic infections and because the recent use of heparin seems to be of theoretic and practical value in prevention of the spread of septic emboli, in stabilization of a clot and in prevention of further thrombosis, it was thought worth while to report a case of particularly severe staphylococcic thrombosis of the cavernous sinus in which treatment with heparin and the sulfonamide compounds was successful.

REPORT OF CASE

T. N., an Italian woman aged 20 years, picked a pimple on the left side of her forehead on Sept. 10, 1942. Later in the day she complained of pain and discomfort in her head and left eye. On September 11 pain was still present, and both lower eyelids were swollen and "flushed," particularly the left. She was admitted to the Utica General Hospital on this date.

On admission the oral temperature was 105.4 F., the pulse rate 142 and the respiratory rate 24. A small furuncle was present on the left side of the forehead. There was pronounced edema of the lids of the left eye and of the upper lid of the right eye, with chemosis of the inferior bulbar portion of the conjunctiva of the left eye. The veins of the nose were congested. The face was slightly edematous. The ears were normal. The Kernig and Brudzinski signs were elicited, and ankle clonus was present. A roentgenogram of the nasal sinuses was negative for sinusitis, nor was there any clinical evidence of such a condition. The patient was acutely ill.

The ocular changes became progressively worse Within forty-eight hours both eyes showed severe proptosis, edema of the lids and chemosis. Lumbar puncture, done on September 13, revealed 2,206 cells in the spinal fluid (mostly polymorphonuclear leukocytes) per cubic millimeter. Staphylococcus aureus was grown from cultures of the spinal fluid. On September 14 a diagnosis of thrombosis of the cavernous sinus was made. On this date a blood count showed 22,800 leukocytes, with 88 per cent polymorphonuclear neutrophils.

Intensive treatment against the infection was then instituted. Sulfathiazole, previously given by mouth, was also administered intravenously in amounts so that the concentration in the blood reached 20 mg. per hundred cubic centimeters. Also, large doses of sulfadiazine were given by mouth because this drug is said

1. MacNeal, W. J.; Frisbee, F. C., and Blevins, A.: Thrombophlebitis of the Cavernous Sinus, Arch. Ophth. **29**:231 (Feb.) 1943.

2. MacNeal, W. J.; Frisbee, F. C., and Blevins, A.: Bacteriophage Therapy of Staphylococcic Septic Obstruction of the Cavernous Sinus, Arch. Ophth. **29**:341 (March) 1943.

3. Schall, L. A.: Treatment of Septic Thrombophlebitis of the Cavernous Sinus, J. A. M. A. **117**:581 (Aug. 23) 1941.

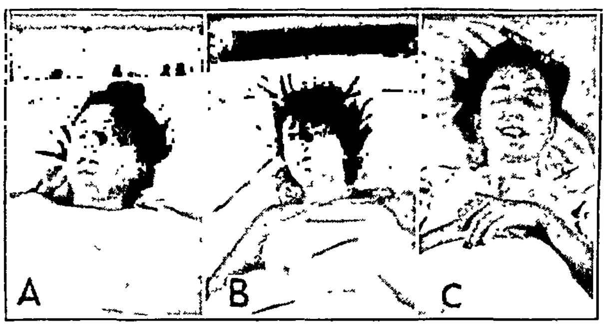
4. Ershler, I. L., and Blaisdell, I. H.: Massive Hematuria Following the Use of Heparin in Cavernous Sinus Thrombosis, J. A. M. A. **117**:927 (Sept. 13) 1941.

to enter the spinal fluid in concentrations up to 65 per cent of that in the blood.

To prevent further thrombosis, heparin solution was given in doses of 10 cc. (10 mg., or 1,000 units, of heparin), diluted in 750 cc. of isotonic solution of sodium chloride U. S. P. A total of 45 cc. (45,000 units) was given during the first month of hospitalization. The coagulation time of the blood was increased to fifty-five minutes.

The patient received 150.5 Gm. of sulfathiazole during a period of five weeks and 498 Gm. of sulfadiazine during a period of four months.

The eyes, which were conspicuously proptosed and immobile, received almost continuous treatment with boric acid compresses. Boric acid ointment and ointment containing butacaine sulfate, 2 per cent, and metaphen, 1 : 3,000, were used to protect the corneas and to combat pain. Several times a day the lids were pulled down over the corneas and held in place with adhesive tape and eye patches.



Photographs of the patient. *A,* during the third week of her illness. The severe proptosis and edema of the lids are evident. The left eye is involved more than the right. *B,* during the fifth week of her illness. The palsy of the left side of the face is apparent. *C,* during the tenth week of her illness. The right eye is nearly normal. The left eye is still proptosed, and the lids are edematous. Only a trace of the palsy remains on the left side of the face. The patient's general nutritional condition has improved (compare with *B*).

Transitory paralysis of the left facial nerve occurred during the fifth week. This gradually cleared up. The temperature fluctuated between 100 and 104 F. for eight weeks. During the eleventh week it fell to 99 F., after which time it was essentially normal.

The proptosis and chemosis of the right eyeball and the edema of the lids of the right eye slowly decreased, and the ocular movements improved so that this eye and its adnexa were essentially normal after the tenth week. In the left eye there developed a superficial opacity of the cornea, due to exposure. Some proptosis and chemosis and pronounced limitation of motion were still present when the patient left the hospital, on Feb. 27, 1943.

At no time was there edema of either disk. The fields were always normal in confrontation tests.

Owing to the prolonged fever, the patient became rather emaciated. Supportive therapy included intravenous injections of dextrose, the use of the Levine tube for introduction of milk, broth and fruit juices into the stomach and administration of aminoacetic acid, vitamins and iron, copper and liver products. She was discharged on February 27, in relatively good physical condition, after a sojourn in the hospital of more than twenty-four weeks.

On March 2, the results of ophthalmologic examination (Dr. Walter F. Duggan) were as follows: Vision in the right eye was 20/15; in the left eye it was 20/200 without correction, 20/160 with + 1.00 D. cylinder, axis 180 and 20/120 with a stenopeic aperture. The right eye was normal, both internally and externally, except for a trace of chemosis at the inner canthus. The pupil measured 3 mm. and reacted directly and consensually to light. The palpebral fissure measured 6 mm.; with a maximal effort to open the eye it measured 12 mm. The extraocular muscles were normal. The left eye was moderately proptosed. A long horizontal fold of chemotic conjunctiva lay just below the cornea. In the cornea were two superficial horizontal opacities, one of which extended across the center of the pupil and was the cause of the lowered visual acuity of this eye. The pupil was 6 mm. in diameter and did not react either directly or consensually to light. The disk and the retinal vessels were normal. As a result of ptosis on this side the palpebral fissure measured 2 mm.; with a maximal effort to open the eye it measured 8 mm. The patient could abduct the left eye 35 degrees and adduct it 20 degrees. The vertically acting rectus muscles and the inferior oblique muscle were completely paralyzed. The superior oblique muscle showed a trace of function.

CONCLUSIONS

In a case of staphylococcic thrombophlebitis of the cavernous sinus treatment was successful with sulfathiazole, sulfadiazine and heparin.

As compared with the amount of heparin given in 4 other cases, only a small amount (45,000 units) was used in the case reported.

It will be neceasary to give heparin in a larger number of cases before its value can be determined. Theoretically, its use is indicated in cases of this condition.

1301 Corlies Avenue.

INFECTION OF LYMPHOID TISSUE OF THE PHARYNX AND OF THE CONJUNCTIVA

RICHARD WALDAPFEL, M.D.

GRAND JUNCTION, COLO.

The anatomic structure of the pharyngeal mucous membrane is characterized by the ample occurrence of lymphocytic elements. They appear singly or in aggregations and in certain nodular formations, which are called lymph follicles. Regular arrangements of such follicles are called tonsils. No matter whether they represent real tonsils or other aggregations of lymphoid tissue, they are homogeneous formations with identical histologic structures, in their entirety called the lymphoid apparatus of the pharynx, and they act alike both in anatomic and in pathologic respects. The acute inflammation of this lymphoid apparatus is called tonsillitis, or angina, the latter name being more comprehensive than the former.

The same kind of lymphoid tissue is present in the conjunctiva of the eye. It appears after the third month of life and is rather thin, in accordance with the minor thickness of the conjunctiva, forming a superficial adenoid layer over the conjunctiva and showing its main formation in the fornix of the conjunctiva.

On the basis of the anatomic analogy between the lymphoid structure in the pharynx and that in the conjunctiva, it was obvious to expect an analogy between the infections involving the lymphoid tissues in the two regions. Two previous reports [1] have confirmed this opinion, with verification by microscopic observation in 1 case. The simultaneous occurrence of infections in the two organs would prove most definitely the analogous character of the infections. I could not find an instance of such an occurrence in the literature available. The 2 cases here reported appear, therefore, of special significance.

REPORT OF CASES

CASE 1.—Mrs. H. L. W., aged 36, complained of soreness and "mattering" in the right eye during the preceding two days. The disturbance started simultaneously with a sore throat, and she still had some difficulty in swallowing and in general was not feeling well.

Eyes.—Examination showed that the left eye was normal. The right eye (figure, *A*) had a mucopurulent discharge; the caruncle was reddened and somewhat enlarged, and the adjacent portion of the conjunctiva of the fornix had the appearance of a thick, infiltrated, spindle-shaped cord, most conspicuous in the nasal portion of the fornix. Very small yellowish points, representing minute infected subepithelial lymph follicles, were shining through the epithelium. The vessels of this part of the conjunctiva were slightly dilated. The rest of the bulbar conjunctiva and the palpebral conjunctiva of the lower lid showed less injection; the conjunctiva of the upper lid appeared fairly normal. The cornea and the remaining sections of the eye were without noticeable pathologic changes. The temperature was 100 F.

Pharynx.—The tonsils were small; the pillars were reddened, and the crypts contained yellowish plugs. Back of each tonsil a longitudinal, dark red swelling of the pharyngeal mucous membrane, with yellowish spots, was visible. These spots were infected subepithelial lymph follicles within bilateral longitudinal aggregations of lymphoid tissue in the posterior pharyngeal wall, known as lateral lymphoid cords of the pharynx, which were infected in the same way as the pharyngeal tonsils.

Diagnosis.—The diagnosis was pharyngeal tonsillitis and infection of the lateral lymphoid cords of the pharynx. *D* of the figure is a photograph of the right half of the throat, showing the infiltrated lymphoid tissue (dark) and numerous infected lymph follicles, appearing as white spots in the darker area.

Course.—Sulfadiazine was given internally, and sulfathiazole ointment was applied locally to the conjunctival sac; within two days both the pharyngeal and the ocular condition had returned to normal.

CASE 2.—W. E. S., a man aged 54, stated that his right eye had been sore and swollen for the past three days. The ocular trouble started at about the same time as did a sore throat. He was feeling sick in general. A similar trouble had occurred in the same eye three years before.

Eyes.—The left eye was normal. The upper lid of the right eye (figure, *C*) was edematous. The conjunctiva of the upper lid and of the bulb was injected, and the temporal portion of the fornix was swollen. In the temporal half of the palpebral conjunctiva of the upper lid two yellowish spots were visible. These yellowish spots were subepithelial abscesses of the lymph follicles, which have previously been described,[1a] and belonged to the conjunctiva, with which they could be moved. Each yellow spot was surrounded by a slightly inflamed halo. Some mucopurulent discharge was present.

Pharynx (figure, *B*).—The tonsils had been removed years before. A small tonsillar tag had been left in the upper portion of the right tonsillar fossa. On the tag, which was swollen, three yellow subepithelial spots could be seen, each one surrounded by a narrow inflamed zone. Below them, in the lymphoid tissue of

1. Waldapfel, R.: Abscess-Forming Follicular Conjunctivitis, Arch. Ophth. **27**:929 (May) 1942. Rigg, J. P., and Waldapfel, R.: Acute Abscess of the Lymph Follicles of the Conjunctiva, ibid. **22**:882 (Nov.) 1939.

the posterior pharyngeal wall, were several spots which were considerably smaller but otherwise of the same appearance. All were strictly limited to the lymphoid tissue of the pharynx and represented miliary abscesses within the lymph follicles, as was described previously.[2]

Course.—The temperature was 100.2 F. Sulfadiazine, administered internally, and sulfathiazole ointment, instilled into the right eye, restored the condition of the eye and the pharynx to normal within two days.

COMMENT

The 2 cases had in common simultaneous infections of the lymphoid tissue of the conjunctiva and of the pharynx. The clinical pictures left no doubt of the relation of the pathologic changes in the two areas and of the identical pathogenesis of the conjunctival and the pharyngeal process.

This infection of the conjunctiva, which corresponds to tonsillitis, or angina, of the pharynx, might justly be named angina of the conjunctiva

A (case 1), infiltration of the lower fornix of the conjunctiva of the right eye, with a few minute infected lymph follicles; *D* (case 1), infiltration of the right side of the pharyngeal mucous membrane, which appears dark, with numerous infected subepithelial lymph follicles; *C* (case 2), two abscessed subepithelial lymph follicles within the palpebral conjunctiva of the upper lid of the right eye, and *B* (case 2), three abscessed subepithelial lymph follicles within a tonsillar tag in the right side of the throat and in several small ones within the lymphoid tissue of the posterior pharyngeal wall on the same side.

These photographs are black and white prints from kodachrome transparencies.

if the name "angina," since ancient times, had not been reserved for changes in the throat accompanied by signs of obstruction. In a previous report,[1a] therefore, I suggested the name "abscess-forming follicular conjunctivitis" for this type of conjunctival infection, on the basis of its microscopic picture, which is characterized by the occurrence of miliary abscesses in the lymph follicles of the conjunctiva, analogous to the abscesses in the lymph follicles of the pharynx associated with acute tonsillitis.

This acute infection of the conjunctiva, according to the foregoing reports, is a disease entity which may appear clinically in the eye associated with the following symptoms: (1) diffuse swelling of the fornix and (2) yellowish spots representing abscessed follicles, single or multiple, in the conjunctiva of the palpebra or of the bulb surrounded by an inflamed halo and covered with epithelium. With both a variable amount of discharge, injection of the conjunctiva, chemosis, edema of the lids and photophobia are present

In view of these observations, attention to the eyes may be indicated in cases of acute infection of the lymphoid tissue of the pharynx and vice versa. It is not at all improbable that a number of cases of conjunctivitis accompanying infection of the pharynx may prove to be coordinated infections with the same cause.

This discussion is likely to revive an old hypothesis. In the years following World War I controversies on the "tonsil problem" were much in vogue in Europe. In those days, Johannes Fein, an Austrian army surgeon, proposed the theory that tonsillitis was not an isolated, local disease of the tonsils but a partial symptom of a systemic infection of the lymphoid tissue of the whole body, and the pharyngeal tonsils presented merely the first apparent local manifestation of this general infection.[3] The tonsillitis, according to this theory, was not the basic disease but the secondary localization of an infection which had taken place elsewhere; in the same way, rheumatism, nephritis and appendicitis were all, like tonsillitis, equivalent, coordinated symptoms of the same infection, and not the after-effects of the tonsillitis. In further consequence of this hypothesis, and to designate the general and systemic character of the disease, he suggested the name "anginosis" instead of angina or tonsillitis, which names designate the pathologic process as a local infection of the tonsils.

This theory experiences in the present report a new confirmation from the ophthalmologic side. Simultaneous infection of the pharyngeal and of the conjunctival lymphoid tissue furnishes evidence of the common etiologic factors and the identity of the infection in the two areas. The pathologic process in the pharynx and that in the conjunctiva appear as equivalent, coordinated manifestations of one infection.

The cases here reported are therefore significant for two reasons: 1. They present an infection of the conjunctiva which is analogous to and identical with the infection of the lymphoid tissue

2. Grossmann, B., and Waldapfel, R.: Lacunar Tonsillitis, Acta oto-laryng **10**:1, 1925.

3. Fein, J.: Die Anginose, Berlin, Urban & Schwarzenberg, 1921.

of the pharynx in tonsillitis. 2. They support the theory that tonsillitis is only part of a general infection of the lymphoid system, rather than a localized infection of the tonsils.

The treatment takes advantage of this knowledge. Both the significant features of the cases just noted point to the existence of a general infection and, therefore, to the use of drugs for general treatment, rather than to the local application of remedies supposed to have a germicidal effect, and used for such action in the past. In fact, Fein demanded, many years ago, that the local treatment of tonsillitis be neglected in favor of the general, internal therapy. The pharmacologist of those days, searching for potent drugs for this purpose, used salicylates, methenamine or mercuric cyanide. Research of recent years has considerably improved the medication. This infection, being of streptococcic origin in the majority of cases,[2] responds favorably, and almost selectively, to the internal use of sulfonamide compounds, so that treatment with these substances seems to be the method of choice. Local therapy may be helpful by producing a mild, useful hyperemia of the diseased parts.

SUMMARY

In the 2 cases reported here infection of the conjunctiva occurred simultaneously with an analogous infection of the pharynx, and both conditions proved to be infections of the lymphoid tissue of identical origin. It appears that there exists a conjunctivitis which is the equivalent of tonsillitis and that some infections of the conjunctiva which accompany infections of the pharynx are to be regarded as coordinate and of the same origin.

De Merschman Gardens.

Clinical Notes

MODIFICATIONS OF THE TONOMETER

JOHN N. EVANS, M.D., BROOKLYN

The general dissatisfaction with the tonometer as a dependable clinical instrument is being voiced with increasing frequency. Its continued employment is justified in that the only other method of estimating pressure, digital palpation, gives results even less accurate and less interpretable.

In 1929-1930 I had occasion to examine for mechanical defects about 100 tonometers of various makes. The great majority of these instruments showed such grave imperfections as to render them well nigh worthless as diagnostic aids. No report of this study was made because the data were too incomplete and the investigation was supplementary to a larger problem, that of "optical tonometry." On careful consideration of the subject, it is obvious that a purely optical means of studying intraocular pressure is highly desirable. No mechanical contact should exist between the eye and the recording device, as the irritation of any foreign substance probably modifies the balance of ocular pressure.

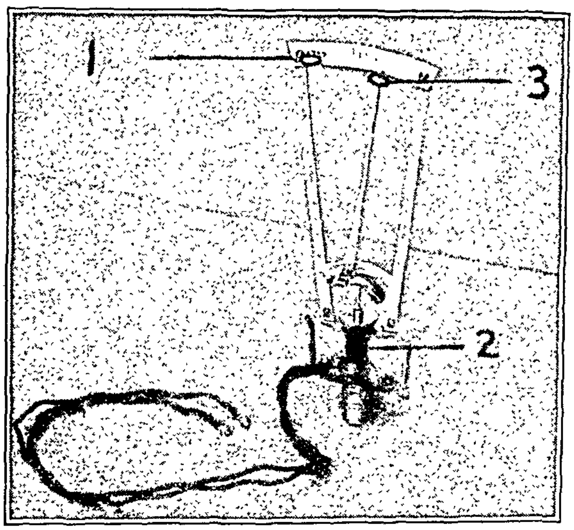


Fig. 1.—*1,* weak plus lens, focusing light from the ophthalmoscope bulb (*2*) on the ceiling as a zero reference point; *2,* ophthalmoscope bulb attached to the finger grip of the tonometer, wires from which connect with a dry cell, clipped on the examiner's wrist; *3,* weak plus lens attached to the pointed focusing light from ophthalmoscope bulb (*2*) on a scale projected on the ceiling.

In the course of protracted studies of this problem, certain modifications of the standard tonometer have been evolved which may in themselves be worth consideration.

In an effort to magnify the standard readings with the Schiøtz tonometer, the instrument shown in figure 1 was evolved. A weak plus lens was attached to the scale and a similar plus lens to the tip of the pointer. An ophthalmoscope bulb was attached to the finger grip as illustrated so that its emitted light impinged on both lenses, irrespective of their relation to each other. An appropriate scale was projected on the ceiling of the room so that it was directly above the tonometer as it was applied to the eye of the reclining subject. A bright point of light was thus projected on this scale by concentration of the light of the ophthalmoscope lamp by the lenses on the tonometer scale and pointer. The projected scale was adjusted until it corresponded

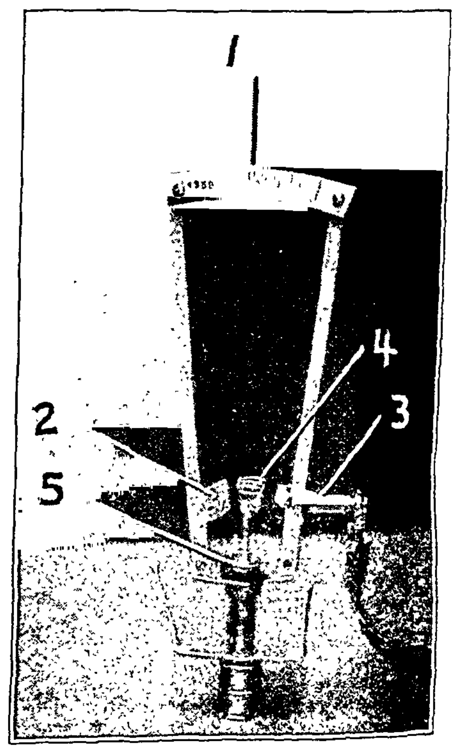


Fig. 2.—*1,* tonometer scale, with attached accessory weights to help in compensating for the pointer, pivot and cam, which have been removed; *2,* counterweight to balance ophthalmoscope bulb (*3*); *3,* ophthalmoscope bulb, projecting light horizontally through the right angle prism-cylindric lens combination (*4*); *4,* right angle prism-cylindric lens combination, which deviates light from the ophthalmoscope bulb and focuses it as a sharp line on the tonometer scale (*1*); *5,* modified tonometer weight to compensate for added prism lens (*4*). Wires from the ophthalmoscope bulb are connected to a single dry cell, mounted by a clip on the wrist of the examiner.

to the stationary point of light. The spot of light projected by the lens on the needle then recorded the movements of the needle with great magnification. Ocular pulsations were thus easily studied. Modifications in the weight of the tonometer were made so that the final instrument was equivalent in weight to the original one.

SECOND MODIFICATION

Another series of changes resulted in the elimination of three moving parts which were the most common source of mechanical defects in the instruments examined. By removal of the pointer, its pivot and the sliding cam against which the tonometer rod operated, a tonometer with only one moving part was obtained.

In order to record the rise and fall of this rod, a prism-lens combination was mounted on the rod in such a way that light from the attached ophthalmoscope bulb, in striking the face of the prism, was deviated vertically and focused on the scale by a cylindric lens mounted on the upper surface of the prism. This arrangement resulted in a pencil of light which acted as a recording needle, with the prism-lens as a fulcrum. It thus recorded the readings on the scale in the usual manner. It was necessary to make allowances in weight for the loss of the lever, pivot and cam and to make other allowances for the weight of the added prism-lens combination; it was also necessary to rebalance the instrument in order to redistribute the shift of weight with the addition of the ophthalmoscope bulb.

In each instrument a small battery attached to the examiner's wrist by a spring clip supplied the current through a delicate flexible cable.

Other models of the tonometer with but one moving part are in the course of development.

It seems fair to assume that certain mechanical defects in standard tonometers have been eliminated in this instrument.

23 Schermerhorn Street.

AXIS FINDER CHART

Captain Philip L. Masor, Medical Corps, Army of the United States

Ophthalmologists have long sought for objective methods of refraction, since the results are reliable and will therefore give the greatest percentage of relief. To further this end, the axis chart which I used in the course of refraction with streak retinoscopy is presented; use of this chart appreciably shortens the examination, at no expense to precision. For patients of all ages, cycloplegic refraction is the most reliable and is the method of choice, and neutralization by plus and minus spheres is the common method.

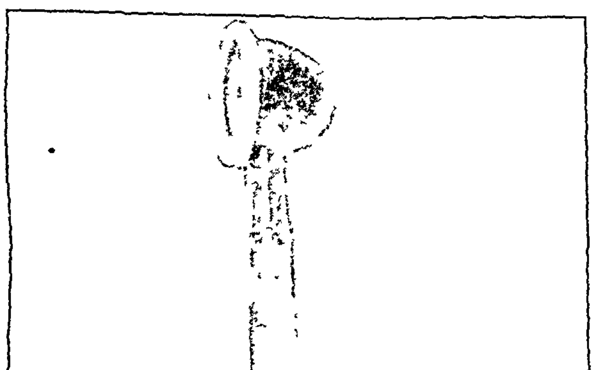


Fig. 1.—Streak retinoscope (Copeland).

I use the method of electric streak retinoscopy (Copeland), which is not as popular as plano-mirror retinoscopy but which has been found to be scientific, reliable and convenient. A few words will describe the simple construction of the streak retinoscope (Copeland).

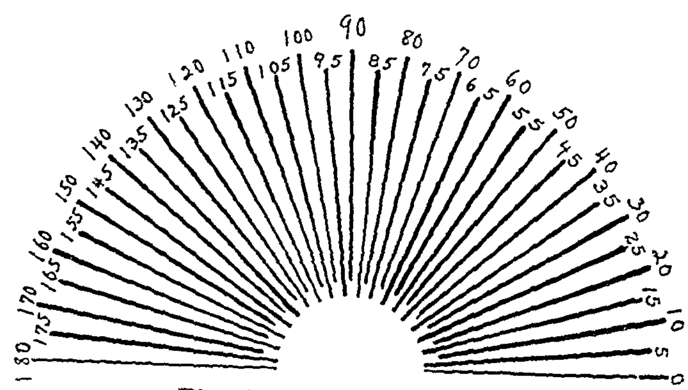


Fig. 2.—Axis finder chart.

STREAK RETINOSCOPY

The streak of light is produced by the specially constructed filament, which is designated in the shape of a hairpin or an inverted, broadly arched U. The condensing lens projects the transverse portion of this filament and produces the image of a straight line. The knurled sliding sleeve on the handle of the instrument varies the width of this streak, and the sleeve may be rotated through 180 degrees, with rotation of the streak.

The refractive error is neutralized with plus or minus spheres. The meridian of least refraction (the smaller error) is neutralized first by plus or minus spheres,

and then the meridian of greater refraction. The position of the streak neutralizing the greater error determines the axis of the cylinder. At this stage the latter streak (the neutralizing streak of the greater refractive error) is projected on a chart marked in degrees, which is located on the wall above the head of the patient. The axis is determined within 3 degrees. The objective method of retinoscopy in general is highly favored. The axis thus found by projection is also purely objective and does not in any way depend on the opinion or fancy of the patient.

Each ophthalmologist can prepare his own chart for finding the axis. I suggest a chart drawn on white cardboard 16 by 10 inches (40.6 by 25.4 cm.). The meridians of half an arc are drawn and lined every 5 degrees. The lines should be distinct enough to be seen by the refractionist in a darkened room at a distance of 1 meter. The designations of the meridians should also be readily discernible.

Determination of the axis with use of the chart is reliable and convenient. By virtue of its objectiveness and ease of operation, the time of examination is greatly reduced, as well as labor saved. In the beginning, streak retinoscopy and objective determination of the axis seem difficult, but after a few months of practice, ease of operation and precision are obtained.

It is a recognized procedure that cylinders are also used in conjunction with spheres in determination of the axis. It is not my intention to decry the use of cylinders; rather, I wish to emphasize that, in addition to accuracy, speed is essential in the examination of the thousands of men subjected to refraction on short notice, and who are often quickly moved from one military station to another.

SUMMARY

The axis chart presented here is used to determine the axis of a cylinder in streak retinoscopy (Copeland) when only spheres are used. It is found to be convenient, reliable and labor saving and appreciably shortens the time required for refraction.

IRITIS, RETINAL HEMORRHAGE AND CHANGES IN THE LENS FOLLOWING INJECTION OF TYPHUS VACCINE

Report of a Case

MAJOR EDWARD F. EAGAN AND CAPTAIN HAROLD J. HALPERN,
MEDICAL CORPS, ARMY OF THE UNITED STATES

Ocular manifestations following injections of serum have not been common, although cases have been reported. Mason [1] reported 3 cases in which measurable blurring of the optic disks developed during serum sickness, with gradual return to normal. Brown [2] reported 5 cases in which elevation of the disk and edema of the retina developed after administration of diphtheria antitoxin. These signs subsided in a few days. Bedell [3] described severe and extensive bilateral edema of the retina with superficial hemorrhages, which he attributed to serum sickness following the injection of tetanus antitoxin. This condition cleared up rapidly, leaving few vestiges. Theodore and Lewson [4] reported 1 case of iritis following antipneumococcic serum.

The case reported here is unusual because it involved damage to the iris, lens, optic nerve and retina without any serum sickness or other prodromal symptoms.

A white soldier aged 22 walked into the ophthalmic clinic complaining of poor vision in the right eye of one week's duration.

The history revealed that he had never had any ocular trouble or systemic disease. He had been in the Army twenty-two months and had had the usual injections of tetanus antitoxin and typhoid vaccine, about four days after induction, to which there had been no untoward reaction. Vision at the time of enlistment was 20/20 in each eye. He had had no previous trouble during training. One week before his admission to the clinic he received his first injection of typhus vaccine, 1 cc., routine before overseas duty. Thirty-six hours later he noticed that his right eye was red and painful. He reported to the ophthalmic clinic of his hospital, where a diagnosis of iritis was made. He stated that vision was blurred at the onset.

Treatment consisted of hot compresses and dilation of the pupil with atropine. The redness and pain subsided, and he was shipped to Camp Kilmer, N. J. He reported to the ophthalmic clinic one week later, complaining that his vision was practically gone.

Examination.—The right eye had no light perception; vision in the left eye was 20/30 + 2, with no apparent refractive error or pathologic process as an etiologic factor. The left eye was normal throughout. The eyelids, cornea and conjunctiva of the right eye were normal; ocular tension was 18 mm. in the right eye and 19 mm. in the left eye. The pupil was dilated and did not respond. The iris was bound down to the lens at 12, 5 and 8 o'clock. The lens showed many small deposits of iris pigment on the anterior surface. The vitreous was cloudy. Examination of the fundus, which was seen with difficulty, revealed only two or three vessels. The disk was not seen clearly, but over the area of the disk was a large, whitish patch, resembling exudate, which extended temporarily to cover the macular area. Because of the hazy vitreous no other details could be made out.

1. Mason, V. R.: Optic Neuritis in Serum Sickness, J. A. M. A. **78**:88-89 (Jan. 14) 1922.
2. Brown, A. L.: Ocular Manifestations in Serum Sickness, Am. J. Ophth. **8**:614-618 (Aug.) 1925.
3. Bedell, A. J.: Stereoscopic Fundus Photography, J. A. M. A. **105**:1502-1509 (Nov. 9) 1935.
4. Theodore, F. H., and Lewson, A. C.: Bilateral Iritis Complicating Serum Sickness, Arch. Ophth. **21**: 828-832 (May) 1939.

The patient was admitted to the hospital and put to bed. A complete medical examination revealed no systemic disease. Laboratory tests, including the Kahn test, chemical studies of the blood and tuberculin tests gave normal results. Examinations of the teeth, ears, nose and throat showed no evidence of any foci of infection. The neurologic examination was negative.

The patient was reexamined five days later, when beginning opacity of the lens was also present. Many whitish interweaving streaks were observed in the anterior portion of the lens.

The patient's condition showed no improvement at the end of three weeks, and he was discharged from the service, with instructions to have follow-up examinations at his nearest veterans hospital.

SUMMARY

This case of iritis, retinal hemorrhage and lenticular changes following injection of typhus vaccine appears to be unique, as no similar case can be found in the literature. Although no follow-up observation was made in this case, there is no question that the extensive permanent damage in the retina will result in loss of vision in that eye.

OCULAR OCCLUDERS

To the Editor:—In the February 1944 issue of the ARCHIVES, *page 170,* Dr. Joseph I. Pascal, in correspondence on a recent article on monocular occlusion from the Dartmouth Eye Institute, writes that "The real purpose of occlusion . . . is to prevent binocular fixation of the object of attention." We believe this is only partly true.

Dr. Pascal has fallen into the same error that many others have when he thinks that partial occlusion is sufficient for a diagnostic or a therapeutic test. In fact, opinions expressed by members [1] of the staff of the Dartmouth Institute in the past have shown that they, too, at one time held the same belief. In our paper [2] on monocular occlusion we point out that reliable and consistent results were obtained only by complete occlusion of one eye, and it is this fact that we wish to stress.

Lancaster never attached any diagnostic importance to the fact that a patient reported no relief when only partial occlusion had been employed. He emphasized the importance of occluding both the central and the peripheral field of one eye in the monocular occlusion test in order to interrupt completely all the phases of binocular vision. Burian [3] demonstrated that peripheral visual stimuli play a large part in binocular vision—so much so that central fixation is disturbed if the peripheral stimuli are sufficiently large and intense.

Many of our patients reported that the least bit of light coming into the occluded eye caused discomfort, whereas with more complete occlusion they were quite comfortable. Dr. Lancaster used monocular occlusion two or three times for therapeutic reasons to once for diagnostic purposes. One of his patients, for whom he prescribed an opaque contact lens for one eye, reported having complete comfort for several months, but returned when headaches began to recur. It was found that a small peripheral piece of the enamel, used to make the contact lens opaque, had been chipped off, so that light could enter the eye. When the enamel was replaced and the lens again made completely opaque, the patient's symptoms were relieved.

Dr. Pascal is quite right when he says that an inconspicuous occluder is an advantage. Certainly, this should be of no great concern when the complete occluder is to be used for diagnostic purposes, and is to be worn for only two weeks. Other things being equal, the less conspicuous the occluder, the better, but to sacrifice the purpose of occlusion for the sake of appearance is advocated only by those who are not aware of the fact that they are making such a sacrifice.

Partial occlusion results in many failures in diagnostic as well as therapeutic use, and, what is more important, it often gives misleading information. An occluder which will interrupt binocular coordination as completely as possible is by far the best for the purpose of predicting whether or not a patient's symptoms are due to a binocular anomaly. In many cases a complete occluder is the only means of obtaining continued relief from an uncorrectible binocular difficulty.

KENNETH L. ROPER, M.D., AND
ROBERT E. BANNON, B.S.,
Hanover, N. H.

Dartmouth Eye Institute.

1. Bielschowsky, A.: Congenital and Acquired Deficiencies of Fusion, Am. J. Ophth. **18:** 933 (Oct.) 1935. Burian, H. M.: Clinical Significance of Aniseikonia, Arch. Ophth. **29:** 131 (Jan.) 1943.
2. Roper, K. L., and Bannon, R. E.: Diagnostic Value of Monocular Occlusion, Arch. Ophth., this issue, p. 316.
3. Burian, H. M.: Fusional Movements: Role of Peripheral Stimuli, Arch. Ophth. **21:** 486 (March) 1939.

CORRECTION

In the abstract of the article by Dr. W. Guernsey Frey entitled "Monocular Exophthalmos Due to Hyperthyroidism in a Patient with the Duane Syndrome" in the report of the November 15 meeting of the New York Academy of Medicine, Section of Ophthalmology, which appeared in the January issue (ARCH. OPHTH. **31:** 116, 1944), the penultimate paragraph should read:

"It appears that when hyperthyroidism developed, the left eye did not become exophthalmic to the same degree as the right, because of restraint exercised by a fibrotic external rectus muscle. *That there was a strong factor favoring proptosis of this eye seems manifest by the swelling of the soft tissues of the globe observed in the eyelids.*"

News and Notes

GENERAL NEWS

Examinations for Technicians, American Orthoptic Council.—The next examination for technicians to be given by the American Orthoptic Council will be held in September and October 1944.

The written examinations will be held at various cities in the country on Sept. 7, 1944. Only candidates passing the written examinations will be permitted to take the oral and practical tests, to be given in Chicago, Oct. 7, 1944.

Applications, on the official form, must be received before Aug. 1, 1944.

Communications should be addressed to the American Orthoptic Council, 23 East Seventy-Ninth Street, New York 21.

Postgraduate Course in Neuromuscular Anomalies of the Eyes.—Dr. George P. Guibor is presenting the twelfth semiannual postgraduate course in neuromuscular anomalies of the eye at the Children's Memorial Hospital, Chicago, May 7 to 12 inclusive.

SOCIETY NEWS

***Medical Society* of the State of New York, Section on Ophthalmology.**—The annual meeting of the Medical Society of the State of New York, Section on Ophthalmology, will be held May 10, 1944, at the Hotel Pennsylvania, New York.

The following papers will be presented:

"Treatment of Complications of Cataract Extraction." John H. Dunnington, M. D., New York.

Discussion: E. Clifford Place, M.D., Brooklyn, and Ivan J. Koenig, M.D., Buffalo.

"Ophthalmoscopic Signs of Terminal Hypertension." Arthur J. Bedell, M.D., Albany, N. Y.

Discussion: Searle B. Marlow, M.D., Syracuse, N. Y., and Morris H. Newton, M.D., Little Falls, N. Y.

"Interpretation of Visual Fields in Neurotic Patients." John F. Gipner, M.D., Rochester, N. Y.

Discussion: Thurber Le Win, M.D., Buffalo, and Walter F. Duggan, M.D., Utica, N. Y.

"Evaluation of Newer Drugs Used in Ophthalmology." Walter S. Atkinson, M.D., Watertown, N. Y.

Discussion: Albert C. Snell, M.D., Rochester, N. Y., and Ludwig von Sallmann, M.D., New York (by invitation).

"Progress of the Glaucoma Campaign During the Past Three Years." Mark J. Schoenberg, M.D., New York.

Discussion: Frank M. Sulzman, M.D., Troy, N. Y., and E. Perry Hall, M.D., Oneonta, N. Y.

Association for Research in Ophthalmology, Inc.—The annual meeting of the Association for Research in Ophthalmology, Inc., will be held at the Sherman Hotel, in Chicago, on Tuesday, June 13, 1944.

Members who desire to present papers or to contribute to the program are requested to communicate with Major Brittain F. Payne, The School of Aviation Medicine, Randolph Field, Texas, who is assembling the program.

PERSONAL NEWS

Appointment to Army Medical Library.—Dr. William Thornwall Davis, Washington, D. C., has been made an honorary consultant to the Army Medical Library.

CORRECTION

In the communication by Major H. S. Sugar in the March issue (ARCH. OPHTH. 31: 269, 1944) in the twelfth line of the second column, "for each 8 mm." should read "for each of the 8 mm."

Obituaries

SANFORD ROBINSON GIFFORD, M.D.

1892-1944

The death of Sanford R. Gifford, on February 25, at the early age of 52, after a short illness, was a great shock to his many friends and is an irreparable loss to ophthalmology. It may be truly said that he gave his life to his profession. He was outstanding as a scientist, writer, director of research, teacher and clinician, a remarkable and unusual combination, and his death, as he was approaching the zenith of his career, was a tragedy.

Sanford Gifford was born in Omaha, on Jan. 8, 1892, the son of Dr. Harold Gifford, the eminent ophthalmologist. After graduating at Cornell University, he received the degree in medicine at the University of Nebraska College of Medicine, Omaha, in 1918. During World War I he served as bacteriologist in the United States Army, with the rank of first lieutenant. On his return to Omaha, in 1919, he practiced with his father and was instructor in ophthalmology at the University of Nebraska College of Medicine, becoming assistant professor in 1924. During this period he was active in research and hospital work and gave promise of his future development as a scientist and a clinician. In 1920 articles from his pen began to appear in the special journals—generally on clinical observations and on the bacteriology of the eyes. In 1923-1924 he studied at the University of Freiburg, Baden, and at the Universities of Vienna and Tübingen; there he became acquainted at first hand with the ophthalmology of continental Europe, particularly from the laboratory standpoint, and learned the value of research.

An important decision for his future life was made in 1929, when he moved to Chicago and joined the staff of the Northwestern University Medical School. His talents then came to the fore, and in this important stage in his career he served as professor and chairman of the department of ophthalmology, a position he held at the time of his death. He was head of the department of ophthalmology and a member of the staff of Passavant Memorial Hospital and had served as attending ophthalmologist at Cook County Hospital since 1932.

At Northwestern University his vigorous capacity for constructive administration found congenial and profitable opportunity. He achieved, with a minimum of officiousness and dissension, most satisfactory administrative results in the many opportunities which the large city of Chicago, with its diversified interests, offers.

Dr. Beulah Cushman furnished me with the data on his work at Northwestern.

Dr. Gifford developed the ophthalmic clinic at Northwestern University into an active clinic with a postgraduate course. An organized postgraduate course was offered in 1935 and continued to be given nine months each year, beginning in September. Each class was limited to 8 students. Altogether, 54 students had finished the course when it was discontinued at the close of the 1941-1942 term for the duration of the war. A residency was opened in Passavant Memorial Hospital in 1930 and in Wesley Memorial Hospital in September 1941. A fellowship in ophthalmic surgery was established which was open to the residents in 1939. The undergraduate training was carried on by the staff, except for the ophthalmic clinic at Cook County Hospital, which Dr. Gifford conducted. The sessions at this clinic were very popular, and many of the senior medical students became actively interested in ophthalmology. He was most enthusiastic about all research and encouraged every member of the staff to take up some problem, to the investigation of which he contributed any funds that were needed, as well as his keen interest and knowledge. The department of photography was developed by the help of his special gifts and enthusiasm, and the first exhibit of kodachrome photographs of external diseases of the eyes held at a meeting of the American Academy of Ophthalmology and Otolaryngology was possible through his encouragement and gifts. The aniseikonia clinic was opened in 1941, and two physicians received their training at the Dartmouth Eye Institute through his foresight and gifts to the department.

He had the pen of a ready writer and expressed himself freely and concisely. Dr. Harold Gifford tells me of the significant fact in his brother's education that he originally wanted to teach English literature and that his entire four years of college were devoted to the arts, rather than to the sciences. After teaching for a year at the University of Omaha, he decided to study medicine, and it was necessary for him to cram in his

premedical science courses at a terrific rate. In the medical school he was an honor student, but had to stay up late at night with his studies. He would frequently go to sleep in class, and there is an old joke in Omaha that "Sandy" knew more when he was asleep than the rest of the students did when they were awake. His ability as a teacher and writer goes back to this earlier training in English literature.

and up-to-date information. The "Textbook of Ophthalmology" contains a wealth of clinical material and experience, formulated in a clear, concise and by no means dry manner. In his research work, he never lost sight of its practical bearing. He was particularly interested in bacteriologic problems and in the biochemistry of the lens. With Dr. J. M. Patton, he reported the probable etiologic agent of the hitherto un-

SANFORD ROBINSON GIFFORD, M.D.
1892-1944

In addition to many monographs on the bacteriology of the eyes, especially diseases due to fungi and the higher bacteria (Diseases of Eye and Adnexa Due to Fungi and Higher Bacteria, Arch. Ophth. 57: 224 [May] 1928), Gifford was the author of "A Hand-Book of Ocular Therapeutics" (Philadelphia, Lea & Febiger, 1937) and "A Textbook of Ophthalmology" (Philadelphia, W. B. Saunders Company, 1938). The book on "Ocular Therapeutics" is the standard work of reference in the English language and is an indispensable source of accurate

known disease agricultural conjunctivitis. At the same time, any clinical problem which presented possibility for research in its elucidation was eagerly grasped. He had been associate editor of the Archives since 1928 and was corresponding editor of the *Klinische Monatsblätter für Augenheilkunde*. His loss to the Archives is enormous, not only on account of the many contributions that he and his staff made, but for his ever present readiness to help and to work. He had an excellent knowledge of several languages and an unusual grasp of medical, especially oph-

thalmologic literature. Diseases of the fundus, which revealed his interest in the problems of general medicine, were of great attraction to him; of articles on this subject, his recent publications on "Central Angiospastic Retinopathy" and "Vascular Retinopathy" are notable. He was a sound surgeon, with excellent judgment and operative skill, and he devised several new procedures for the correction of ptosis and other muscular defects.

Gifford was a member of the American Ophthalmological Society, the American Academy of Ophthalmology and Otolaryngology, the Association for Research in Ophthalmology, Inc., the American College of Surgeons and the Institute of Medicine of Chicago.

Gifted in mental powers of a high order, he added to these industry, determination and imagination and in a relatively short life achieved unusual eminence in his profession and made permanent contributions to ophthalmology. There is no branch of his specialty that did not interest him and to which he did not contribute. As a teacher and lecturer he had unique gifts. In public speaking his presentation was clear and to the point and was delivered with sincerity and dignity, and with just the right touch of humor. His energy was untiring and enabled him to carry on the enormous amount of work which his daily routine demanded.

The many qualities that helped to make Sanford Gifford the outstanding man he was were most apparent. It is not strange that his charm of manner and his forthcomingness drew men to him. He was a man of taste, culture and wide interest and was appreciated not only for his skill but for his straightforwardness, kindliness and tact. He was fortunately blessed with a family life of singular happiness. He is survived by a wife, who stood by his side with understanding heart and wise counsel, and by 2 sons, the older, Sanford R. Jr., a physician, and the younger, Carter, an architect, who are both in military service. Those who have known and worked closely with Sanford Gifford are mourning a dear friend with memories of deep affection and of high regard, and the medical profession has lost an outstanding personality.

ARNOLD KNAPP.

With the passing of Sanford Gifford ophthalmology has lost a brilliant scientist and I have lost an intimate friend. To those who knew him well he was known as "Sandy," and it is to "Sandy" as a friend that I wish to pay my tribute.

In 1922, when I attended my first meeting of the Section on Ophthalmology of the American Medical Association, in St. Louis, alone and without an acquaintance, it was "Sandy" Gifford who took me under his wing and saw to it that I enjoyed the meeting. From this developed a friendship that became more intimate through the years. I have spent many pleasant hours as a guest of "Sandy" and his gracious, charming wife, and have thus seen their beautiful home life and the happiness they derived from their two sons.

In 1939 "Sandy" became a member of the Bohemian Club of San Francisco and started attending the midsummer encampments in the club's 3,000 acre redwood grove, 60 miles north of San Francisco. Since we were members of the same camp, it was here, away from the hurry, tension and responsibility of daily routine, that I learned to know him well. It was during the first, more quiet, part of the encampment that we had many intimate talks, while going to the swimming hole, walking through the forest or sitting around the campfire at night. It is the memories of these hours that seem most dear, for it was here that at close hand I observed the qualities that endeared him to all who knew him.

He was first of all a scientist and an ophthalmologist, but it is as a great clinician that most of his associates will remember him. He always had an open mind and was ever ready to acknowledge the good in others' work. If he adopted a new procedure, he was most careful to give credit where credit was due. "He was so gentle and wisely just in all his dealings," kind and considerate of others and, above all, charitable toward the weaknesses and failings of his fellow man and fellow practitioner. His modest, unassuming bearing, combined with a sincere interest in the welfare of the younger men, endeared him to them. They had a profound respect for him but were always at ease in his presence.

Beneath the serious exterior was a keen sense of humor, which is well illustrated in his delightful account of his experiences in his father's office in Omaha. To this paper, which he read before the Chicago Literary Club, he gave the title, "Garlic and Old Horse Blankets (Being Some Presenile Reminiscences by Sanford R. Gifford)."

In addition to his attainments in ophthalmology, "Sandy" had an appreciation of literature and music. Reading was one of his favorite means of relaxation. I have a highly prized

photograph of him taken at the grove in his favorite spot in camp, dressed in shorts, semi-reclined on a "sun chair," smoking his beloved pipe and reading a book on the history of Greece. He never tired of music and always looked forward to the evening concerts out under the redwoods or at the lake.

To have known "Sandy" as a colleague, as a camp mate and, above all, as a comrade has been a rare privilege. The memory of those associations will continue to be an inspiration, not only to greater attainments in ophthalmology, but to the finer things in life.

In a little while there will be another midsummer encampment. The ageless redwoods of the forest, the swimming hole, the camp and the nights before the fire await me as of yore, but it will not be the same. "Sandy" will not be there.

FREDERICK C. CORDES.

Words cannot portray the rare personality we knew as "Sandy." Gentle, kindly, modest and self effacing, he possessed great strength. Out of his vast reservoirs of intellectual power there poured numerous contributions to the science of ophthalmology, painstaking care of patients and teaching that was both accurate and stimulating.

But he was far more than an accomplished specialist. Had he devoted himself to literature he would have added much to the prestige of American letters. Among my most prized possessions are a few verses which are worthy of the immortal Keats. He inscribed them—long ago—to his mother on her birthday. Few equaled his natural flair for writing. His mind pictured at once every facet of scene and incident. His seriocomic essay "Garlic and Old Horse Blankets" (privately printed, 1943) will endure. Its very whimsicality reflects a playful mood which rarely deserted him.

It seems as though I had known him always. He wasn't much more than 10 when I first glimpsed the spindling lad who was so adventurous, so curious. His parental home was the gathering place for the neighborhood youngsters. Although many were older than he, leadership was his by natural right. Only in after years did he relate how, with a companion, he climbed the well of the high school tower, with the narrowest of toe and finger holds offered by jutting bricks and sills.

The spirit of youth never forsook him. His enthusiasm was contagious and his industry the marvel of his colleagues. He thought long thoughts. By temperament, he was an artist.

The ashes of this noble man repose in a quiet spot in far-off California, where—a few years hence—he had hoped to find surcease from the chores of the day, with some leisure for writing. Those who must carry on will not fail to hear his words of encouragement. They will envision his quizzical smile and catch his understanding chuckle.

In all humility we bow before Ultimate Truth, which he exemplified so valiantly.

IRVING S. CUTTER.

CARL KOLLER, M.D.
1857-1944

With the passing of Dr. Koller, it is fitting to emphasize once again the achievement for which he will be remembered—his discovery of the use of cocaine for local anesthesia. This discovery, in 1884, marked the beginning of local anesthesia as it is now known. He was searching for a substance which might be used for this purpose and, while studying the systemic action of the drug, noted the benumbing effect of cocaine on the tongue. This led him to experiment with it for local use. The story has been told many times, but, because of errors and confusion about it which had cropped up in the course of the years, he retold it in detail in 1927, at a joint meeting of the Associated Anesthetists of the United States and Canada and the International Anesthesia Research Society and published his notes in *The Journal of the American Medical Association* (90: 1742 [May 26] 1928) and in a number of European journals.

In his early years, during student and intern days, he worked in embryology in Stricker's laboratory, in Vienna, and published in 1879 and 1882 his observations on the origin of the mesoderm as studied in the chicken embryo. This work represented an original idea he had about the mesoderm, which proved correct on investigation. Dr. Koller thought well of this achievement and spoke of it frequently in his later years. He received his training in ophthalmology in

CARL KOLLER, M.D.
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Vienna under Arlt and in the Eye Hospital in Utrecht, Netherlands, which was then conducted by Professors Snellen and Donders.

He continued to experiment during many years, interesting himself in astigmatism, improvements in the ophthalmometer and other subjects. He devised, among other things, the lighting system now being used in the electric ophthalmoscope. He also wrote many articles on clinical subjects in ophthalmology.

In general, it may be said of Dr. Koller that his mind was essentially scientific, keen and inquiring throughout his long life, although he was a most successful practicing ophthalmologist, noted as an outstanding diagnostician and surgeon. He practiced in New York from 1888 to 1942 and was associated with the Mount Sinai Hospital for many years.

He was not a calm person, nor had he ever any hesitation about expressing criticism, whether of himself or of others, if he discovered error. Like all scientifically minded people, he despised insincerity in medical science and practice and often jibed at it.

To all with whom he came in contact, he was a stimulating personality, always speculating and wondering about the unknown and the unsolved problems in all lines of endeavor. Friends, colleagues and patients sensed in him a real person—true, reliable and fearless—no matter what the surface manifestation.

He was honored by various societies for the work with cocaine, receiving medals from the American Ophthalmological Society, in 1922; the University of Heidelberg, Germany, in 1928; the New York Academy of Medicine, in 1930 (it's first award), and the American Academy of Ophthalmology and Laryngology, in 1934.

Also, he received a scroll of recognition from the International Anesthesia Research Society and honorary membership in a number of societies here and in Europe.

Dr. Koller was a credit to his chosen profession, and his work remains a boon to mankind.

SELINA BLOOM.

CHARLES EDWARD FINLAY, M.D.

1868-1944

Dr. Charles Edward Finlay died at the age of 76 in his home in Habana, Cuba, on March 17, after a prolonged illness. He was born in Habana, the son of the celebrated Dr. Carlos J. Finlay, who was closely identified with yellow fever research. After his graduation from Columbia University College of Physicians and Surgeons, in 1889, he was connected with the New York Ophthalmic and Aural Institute from 1889 to 1892, as an assistant to Dr. Herman Knapp. He then returned to Habana and began an active career. He received the degree of Doctor of Medicine from the University of Habana in 1900 and was a member of the board of directors of No. 1 Hospital, Habana, and of the Central Board of Charities. He began to teach at the Habana Medical College in 1904, became professor of diseases of the eye, after a competitive examination, in 1907. He was director of charities in Habana in 1921-1922; president of the executive committee of the First National Cuban Medical Congress in 1921; delegate for Cuba to the International Congress of Ophthalmology, Washington, D. C., in 1922; honorary president of the Seventh National Cuban Medical Congress in 1924, and vice president of the Habana Medical College in 1925. He became a member of the American Ophthalmological Society in 1927. In 1933 Dr. Finlay returned to the United States and became research fellow at the Eye Institute of the Presbyterian Hospital for one year, in 1933. In the same year he was appointed director of charities in Cuba and received the Grand Cross of the Finlay Order.

He served as dean of the medical school of the University of Habana from 1934 to 1937. In 1938 he became identified with sanitation; he acted as health officer for Habana in 1938 and director of public health for Cuba in 1939; he was a member of the American Public Health Association and represented Cuba at the meeting of the Public Health Congress in Washington, D. C., in 1940. In 1941 he was elected vice president of the American Public Health Association and emeritus professor of ophthalmology in the University of Habana.

Dr. Finlay was a frequent contributor to the special journals on ophthalmology, and many of his publications and abstracts from the South American journals of ophthalmology appeared in the ARCHIVES. His articles were generally of a clinical nature. One of his interesting observations was entitled "Bitemporal Contraction of the Visual Fields in Pregnancy" (ARCH. OPHTH. 52:50 [Jan.] 1923). He wrote on his father's work in connection with yellow fever on a number of occasions and published a book entitled "Carlos Finlay and Yellow Fever," which appeared in New York in 1940. His translation into Spanish of May's "Manual of Diseases of the Eye" was published in Habana in 1939. Many of his recent papers were concerned with sanitation and public health.

Dr. Finlay was modest and hard working. He lived a useful life in his home city of Habana, occupying a number of civic positions, in addition to carrying on an active practice, and as teacher of ophthalmology he undoubtedly contributed to the appreciation of American ophthalmology in Cuba.

He leaves a wife, five daughters and two sons.

ARNOLD KNAPP.

ADOLPH O. PFINGST, M.D.

1869–1944

Dr. Adolph O. Pfingst, the dean of Kentucky ophthalmologists, died on February 25, aged 75, of coronary occlusion, at his home in Louisville, Ky. He was the son of H. Adolph Pfingst, pioneer druggist in that city. After graduating from the Louisville High School, he received studies in ophthalmology under Professors Uhthoff and Axenfeld. In 1893-1894 he worked in the University Eye Clinic in Berlin and at the same time wrote his thesis for the degree of Doctor of Medicine from the University of Berlin. In 1895 Dr. Pfingst returned to this

ADOLPH O. PFINGST, M.D.
1869-1944

his degrees of Bachelor of Arts and Doctor of Medicine from the University of Louisville. He interned at the Louisville City Hospital and filled a part term at Mt. Sinai Hospital, New York. He then went to Europe to take up the study of ophthalmology. After spending a year in the study of pathology and bacteriology at Marburg, Germany, under the guidance of Professors Marchand and Fraenkel, he began his country and became house surgeon to Dr. Herman Knapp at the New York Ophthalmic and Aural Institute for one year. After this thorough training he returned to his home town and established himself as an ophthalmologist, continuing his work in the bacteriologic and histologic laboratories. In 1906 he was appointed professor of ophthalmology in the University of Louisville and director of the ophthalmic clinic

at the Louisville City Hospital, which position he occupied until 1938, when he retired with the title of professor emeritus.

Dr. Pfingst was a member of the American Ophthalmological Society and served on the council for a number of years. He was a member of many other special and general societies. He was always interested in civic affairs; he organized the first sight-saving class in Louisville and was active in the national movement for the prevention of blindness.

He made a number of important contributions to scientific medical literature on subjects usually connected with the pathology of the eye and on diseases and anomalies of the intracranial blood vessels.

He is survived by his wife, Mrs. Lula Solger Pfingst. With his training and natural aptitude, Dr. Pfingst became a sound ophthalmologist, thorough and earnest in his work, and was a worthy representative of his specialty. A man of sterling qualities, a kindly and strong personality, a simple, unaffected man of transparent honesty, he will be missed by a large circle of friends.

ARNOLD KNAPP.

Dr. Adolph O. Pfingst was one of the few in whom are present all of the attributes necessary to make the ideal physician. Skill and diligence in the practice of ophthalmology, equanimity, humility, humaneness, unselfishness and human understanding—all these were in happy combination.

As a teacher he excelled. Qualifying himself by thorough postgraduate training, unusual fifty years ago, he immediately began a long teaching career. One of his first courses was in bacteriology, for which he wrote his own textbook, no other being available at that time. When ophthalmology and otolaryngology were included in the curriculum, he became an instructor in these subjects, and in time was made professor of ophthalmology and chief of the department in the University of Louisville School of Medicine, which position he held for many years. His favorite method was that of quizzing, during which he learned the names of all his pupils. His memory was such that, years later, when former students called on him in his office, he could call them by their first names. His appearance belied the fact that he was never a man of robust health, and as time passed and his private practice grew large, he reluctantly was forced to give up his teaching. However, his interest in medical education never waned.

It was inevitable that Dr. Pfingst should enjoy a busy private practice, so that many times his strength was sorely taxed to serve all who sought his help. Yet he never became impatient, but always was painstakingly careful to see that each patient was given proper attention. As a result, he was dearly beloved by his many patients.

While his profession came first, Dr. Pfingst had a diversity of interests. He was a lover of music and a follower of all kinds of sports and participated in many civic activities.

One of the most beautiful memories of this great man is his tender devotion to his wife and family. This happy home life encouraged, supported and inspired him throughout his entire career.

To have been the pupil and associate of such a man was a rare privilege indeed.

C. DWIGHT TOWNES.

EDMOND EDUARD BLAAUW, M.D.
1867–1943

Edmond Eduard Blaauw was born in Arnheim, Netherlands, in 1867, the son of a cavalry officer. One of a family of 4 boys, he was brought up near The Hague in a simple and artistic atmosphere. He began his medical studies at the age of 19, at the University of Amsterdam, spending a number of years in study in Freiburg, Germany, and Lyon and Paris, France. He then became assistant to Professor Gunning, at the Amsterdam Eye Hospital, and graduated in 1894, with the publication of a thesis on trachoma. He then married and came to this country, settling in Buffalo.

EDMOND EDUARD BLAAUW, M.D.
1867-1943

Dr. Blaauw was associated with the German Deaconess Hospital and the Buffalo Eye and Ear Dispensary, and was a member of the American Medical Association, the Academy of Ophthalmology and Otolaryngology, the Buffalo Academy of Medicine and the Erie County Society and a number of European societies.

He was a faithful attendant at medical meetings and, beginning with 1900, contributed many articles to ophthalmic journals. Some of the articles were on the physiology and anatomy of the eye, but most were clinical. Illustrative of his interests were the articles entitled "Aging of the Eye," a translation of the views of Vogt and Rochat (Arch. Ophth. 2:468 [Oct.] 1929) and an obituary of Allvar Gullstrand (Arch. Ophth. 5:294 [Feb.] 1931).

He continued his association with European ophthalmologists and frequently attended the meeting of the German Ophthalmological Society, in Heidelberg, and the international congresses. A trip around the world was a particularly important incident in his life and enabled him to visit the hospitals in Japan, China, Netherland East Indies and British India.

In 1941 he broke his hip and then heart trouble developed; this made him more or less of an invalid and led to his death, on Dec. 4, 1943.

Dr. Blaauw was of a studious nature, preferring to spend his spare time in his library, where he had collected 10,000 volumes, in four languages. His knowledge of the literature was exceptional, and he was often called on to look up topics for his colleagues.

An agreeable personality, of great intellectual honesty, he was more interested in the science of ophthalmology than in the practice of it. At the same time, he was an ideal *physician*, unselfish, free from any prejudices and ready to help both rich and poor. Beloved and respected by his colleagues and patients, to whom his death is a great loss, he leaves the *memory of a noble* character and of a striking personality.

Arnold Knapp.

Abstracts from Current Literature

Edited by Dr. William Zentmayer

Comparative Ophthalmology

Choline Esterase in the Amphibian Sphincter Pupillae. P. B. Armstrong, J. Cell. & Comp. Physiol. 20: 47 (Aug.) 1942.

In his studies on the action of acetylcholine on the sphincter pupillae of excised eyes of recently metamorphosed salamanders (Amblystoma opacum and Amblystoma punctatum), the author observed that the threshold for stimulation of the sphincter was considerably higher in eyes in which the cornea was left in place than in eyes from which the cornea had been removed. A marked potentiation of the action of acetylcholine by physostigmine was readily obtained in eyes with an intact cornea and was absent after removal of the cornea. The experimental data appear to indicate that choline esterase is either completely lacking or present only in minute amounts at the parasympathetic postganglionic terminations in the amphibian sphincter pupillae, in contrast to the relatively high concentrations of esterase at most peripheral nerve endings.

L. von Sallmann.

Injuries

An Interesting Case of Rupture of the Choroid. E. Rosen, Brit. J. Ophth. 27: 552 (Dec.) 1943.

After an injury to the right eye by a piece of wood flying, end over end, the pupil became eccentric and partially dilated, the lens was partially dislocated and four tears were present in the choroid. The two smaller tears were situated close to the macula. The second rupture, shaped somewhat like a spear head, seemed very close to the macula. The third and fourth ruptures were typically crescentic. While the author was preparing to report this case, he encountered a second case with four ruptures of the choroid.

W. Zentmayer.

Instruments

Evaluation of Orthoptic Instruments. E. K. Stark, Am. J. Ophth. 26: 1308 (Dec.) 1943.

Stark concludes that the major amblyoscopes (synoptophore, synoptoscope and orthoptoscope) are the instruments preferred. The stereo-orthopter facilitates the development of fusion. The rotoscope affords particularly effective exercise for correction of vertical disturbances.

W. S. Reese.

Lacrimal Apparatus

Dacryocystorhinostomy: The Logical Treatment for Occlusion of the Lacrimal Sac. A. V. Hallum, J. M. A. Georgia 32: 186 (June) 1943.

Hallum concludes that dacryocystorhinostomy is the operation of choice in all cases of occlusion of the lacrimal sac, except when the puncta and canaliculi are occluded or when the sac is involved by a malignant or tuberculous process. The operation has proved highly successful in the hands of many operators, and the surgeon should feel that it is his moral obligation to his patient to reestablish intranasal drainage of the lacrimal sac.

W. Zentmayer.

Lens

Lens Extractions Following Filtering Operation for Glaucoma. S. R. Gifford, Am. J. Ophth. 26: 468 (May) 1943.

Gifford states that his experience with a series of cases of cataract following a successful filtering operation has shown that extraction by the temporal route is a practical method of dealing with the problem. In only 1 case did tension rise appreciably above the level present before cataract extraction, and the filtering scars showed little change. There were no operative complications directly referable to the method.

The article is illustrated.

W. Zentmayer.

Oral Use of Prophylactic Sulfadiazine for Cataract Extractions. J. S. Guyton and Alan C. Woods, Am. J. Ophth. 26: 1278 (Dec.) 1943.

In a series of 312 cataract extractions in which sulfadiazine was used prophylactically, postoperative infection was significantly lower than in two control series of 159 and 642 extractions respectively.

W. S. Reese.

Endophthalmitis Phaco-Anaphylactica. R. C. Scobee and H. C. Slaughter, Am. J. Ophth. 27: 49 (Jan.) 1944.

Scobee and Slaughter give the following summary:

"Herewith is presented confirmation of Burky's work of 1934; namely, that cutaneous sensitivity to lens substance in rabbits can be induced by repeated and coincident injections of staphylococcus toxin and lens substance. When the eyes of such sensitive rabbits are needled, a

clinical and histologic picture develops that resembles endophthalmitis phaco-anaphylactica in man. Our series did not show the cutaneous sensitivity which Burky mentioned, yet end results were the same. We report this confirmation of Burky's work as the first step in a series of experiments having to do with endophthalmitis phaco-anaphylactica and sympathetic ophthalmia."

W. S. REESE.

Methods of Examination

THE USE OF PSEUDO-ISOCHROMATIC CHARTS IN DETECTING CENTRAL SCOTOMAS DUE TO LESIONS IN THE CONDUCTING PATHWAYS. L. L. SLOAN, Am. J. Ophth. **25:** 1352 (Nov.) 1942.

Sloan recommends Ishihara charts for the quick and simple detection of central scotoma, the charts being viewed from a distance of 1 meter. She feels that these charts constitute a reliable test but that normal responses do not rule out the presence of a central scotoma.

W. S. REESE.

ENTOPTIC METHODS IN CLINICAL INVESTIGATIONS. B. FRIEDMAN, Am. J. Ophth. **26:** 235 (March) 1943.

This interesting article suggests that more use should be made of entoptic phenomena in determination of intraocular disease when opaque media do not permit ophthalmoscopic examination.

W. S. REESE.

RETROILLUMINATION. R. I. LLOYD, Am. J. Ophth. **26:** 799 (Aug.) 1943.

Lloyd expresses the hope that retroillumination will be made a part of the regular routine of enucleation in ophthalmic hospitals. If this is accomplished, it will soon be known whether tumor can be differentiated from other masses in the fundus.

W. ZENTMAYER.

PRESENT LIMITS OF GONIOSCOPY. P. C. KRONFELD and H. I. MCGARRY, Am. J. Ophth. **27:** 147 (Feb.) 1944.

Kronfeld and McGarry give the following summary:

"The present status of gonioscopy may be summed up by listing some of its plus as well as its minus values.

"Plus values of gonioscopy: 1. Gonioscopy offers a simple mechanical explanation for certain glaucomas. 2. Gonioscopy helps choose the type of operation most suitable for the case under consideration. 3. Gonioscopy helps recognize the causes of failure of glaucoma operations. 4. The information obtained by gonioscopy is of prognostic value in that it enables us to tell whether or not a filtering operation will continue to function. 5. The information obtained by gonioscopy may be of value in inflammatory and traumatic diseases of the eye.

"Minus values of gonioscopy: 1. Gonioscopy offers no explanation of the mechanism of certain glaucomas. 2. Gonioscopy requires some special equipment. From 2 to 4 hours are required to learn the technique of gonioscopy. Considerable experience is required to interpret cases in which the landmarks have been obliterated. 3. Gonioscopy is conducive to the development of an over-mechanical concept of glaucoma."

W. S. REESE.

Neurology

THE PSYCHONEUROTIC FACTOR IN OPHTHALMIC PRACTICE. C. A. BAHN, Am. J. Ophth. **26:** 369 (April) 1943.

Bahn reviewed a series of 400 consecutive office cases, 215 of men and 185 of women. In his opinion a psychoneurotic factor that was capable of effecting symptomatic recovery existed in 301 cases. He gives the following summary:

"The rate of psychoneuroses in ophthalmic practice is 75 per cent compared with 50 per cent in general practice.

"Psychoneuroses involving the eyes are essentially due to imbalance of the autonomic nervous system.

"Symptomatic manifestations are: visual, sensory, secretory, vasomotor and motor disturbances.

"The functional element of the patient's symptoms is usually easily separated from the organic elements.

"Health routines are the only practical treatment of the functional element.

"Health routines integrate all of the fundamentals of physical and mental hygiene in the correct timing, the proper order, and the most intelligent manner.

"A basic health routine is given in detail and its adaptation explained and illustrated by case reports."

W. ZENTMAYER.

CHOKED DISCS AND LOW INTRATHECAL PRESSURE OCCURRING IN BRAIN TUMOR. P. J. LEINFELDER, Am. J. Ophth. **26:** 1294 (Dec.) 1943.

Leinfelder presents the significant data in 12 cases of tumor of the brain, low intrathecal pressure and choked disk. He concludes from the evidence available that the condition in these cases should be considered as true hydrocephalus, the lumbar pressure remaining unexplained except in a few instances.

W. S. REESE.

EXPERIMENTAL STUDIES ON HEADACHE. E. KUNKLE, B. RAY and H. WOLFF, Arch. Neurol. & Psychiat. **49:** 323 (March) 1943.

The authors infer that headache following drainage of cerebrospinal fluid is caused primarily by traction by the brain on various pain-

sensitive structures which anchor it to the cranium; dilatation of some of these structures, the intracranial veins and increase in brain volume are suggested as joint factors in the augmented traction which follows drainage of fluid and leads to headache.

The headache so often associated with increased intracranial pressure has generally been assumed, but never proved, to be related to the increased pressure. Yet (*a*) elevation of intracranial pressure in normal human subjects to abnormally high levels failed to cause headache; (*b*) in a series of 72 patients with tumor of the brain, headache occurred almost as frequently with normal as with increased pressure, and (*c*) headache homolateral to the lesion in a patient with a tumor of the brain was induced by lowering the intracranial pressure, but could not be induced by elevation of the pressure to a high level of 5.5 mm.

Hence in the production of headache, increased intracranial pressure is neither a prime nor an essential factor.

From these data it is concluded that the headache associated with either decreased or increased intracranial pressure results from traction on or displacement of pain-sensitive intracranial structures and is independent of generalized intracranial pressure changes themselves.

R. Irvine.

Bilateral Thrombosis of the Posterior Calcarine Arteries with Sparing of Macular Vision. R. McDonald, Arch. Neurol. & Psychiat. **49:** 484 (March) 1943.

A case of bilateral hemianopsia caused by bilateral thrombosis of the calcarine arteries is presented. The patient had as his only complaint complete loss of peripheral vision. With correction vision was 6/6 in both eyes, and he read Jaeger test type 1 without difficulty. The results of neurologic and medical examinations were essentially normal. The patient had first, second and third grade fusion as tested on the synoptophore, and optokinetic nystagmus was readily elicited in all directions.

The cortical representation of vision and the vascular supply to the area striata are discussed.

First, in all likelihood the macular regions in the occipital pole are frequently supplied by branches of the middle cerebral rather than branches of the posterior cerebral artery. This is important because it at once fixes in mind the reason that with lesions in the temporal lobe there is complete hemianopsia, whereas with lesions of the occipital lobe there is frequently sparing of the macula.

It is concluded that peripheral vision is not essential for stereopsis or spatial orientation and that optic nystagmus may be elicited even if the field is reduced to about 2.5 degrees on either side of fixation. Apparently, the performance of the complex visual functions are dependent on macular fixation and on certain associated pathways which are not closely connected with the cortical areas supplying peripheral vision.

R. Irvine.

Myasthenia Gravis: Curare Sensitivity: A New Diagnostic Test and Approach to Causation. A. Bennett and P. Cash, Arch Neurol. & Psychiat. **49:** 537 (April) 1943.

The authors summarize their presentation as follows:

"1. It appears that some failure in the action of acetylcholine exists in myasthenia gravis.

"2. Physostigmine restores neuromuscular performance in most myasthenic patients.

"3. Curare neutralizes acetylcholine action and produces artificial myasthenia gravis.

"4. There is some evidence that a primary muscle disorder apart from neuromuscular block may occur in certain stages of the disease.

"5. The myasthenic patient exhibits a pronounced sensitivity to curare. One-tenth the usual physiologic dose of curare produces profound exacerbation of existing symptoms, and generalized curarization adds new symptoms of myasthenia.

"6. These phenomena suggest a specific diagnostic test for the disease. Injection of one-tenth the usual physiologic dose of standardized curare is a safe procedure if followed by administration of prostigmine methylsulfate. Larger doses must be administered with caution, as fatalities may occur.

"7. Five patients with different phases of the myasthenic syndrome have shown a specific response to the curare diagnostic test, even though for some the prostigmine test was inconclusive

"8. The cause of myasthenia gravis should be found by explaining the occurrence in the disease of the neurophysiologic disturbance resembling chronic curarization." R. Irvine.

Juvenile Amaurotic Idiocy: A Clinicopathologic Study. A. Lubin and O. Marburg, Arch. Neurol. & Psychiat. **49:** 559 (April) 1943.

A case of the juvenile type of amaurotic family idiocy is described. The results of neurologic, psychologic, encephalographic and histologic studies are correlated, with particular reference to cortical activity. In spite of severe and widespread cellular alterations, many cortical functions were retained, and the electroencephalographic pattern was not especially impaired.

The disorder in this case was typical of the juvenile form of amaurotic family idiocy, from both the clinical and the pathologic aspect. There were: (1) initial onset of visual disturbances between the fifth and the eighth year, progressing

to total blindness in one or two years, with retinitis pigmentosa and optic nerve atrophy; (2) mental deterioration and behavior disturbances, progressive throughout the course of the disease; (3) convulsions, usually beginning fairly late; (4) other neurologic manifestations, such as ataxia, tremors, nystagmus and pathologic reflexes, usually appearing during the terminal phase, and (5) death, from ten to fifteen years after the onset.

From the pathologic picture it may be concluded that cortical alterations consist mainly of (1) diffuse lipidosis and swelling of ganglion cells; (2) completely asystematic, patchlike disappearance of cells, most striking in the third and fifth layers, and (3) sclerosis of the molecular layer, with loss of tangential fibers.

R. Irvine.

Ocular Muscles

Near Horizontal Phoria and Duction Tests S. V. Abraham. Am. J. Ophth. 26: 271 (March) 1943.

Abraham gives the following summary of his study:

"From a detailed study of more than 4,000 cases, 300 typical cases have been presented to show how the various findings from near horizontal phoria and duction tests fall into three characteristic groups: I, the normals; II, the subnormals; III, the abnormals.

"Certain evidence is presented to suggest that, basically, group III may resemble group II.

"The relation of the base-in reading at 13 inches [33 cm.] to the interpupillary distance is emphasized.

"The effect of cycloplegia on the findings is shown not to be dependable even though tendency of cycloplegia to cause a reduction in the convergence activity is suggested."

He draws the following conclusions:

"The possibility of obtaining consistent dependable muscle findings exists, if attention is given to near horizontal phoria and duction tests.

"These findings permit classification, with a resultant opportunity of studying the characteristics of the groups.

"A classification is presented which the author has used for over 10 years with continued proof of its dependability."

W. S. Reese.

A Visual Phenomenon Related to Binocular Triplopia. H. M. Burian, Am. J. Ophth. 26: 1084 (Oct.) 1943.

A man aged 22, a student, had pronounced anisometropia and alternating divergent strabismus, which had undoubtedly existed from early childhood but which he was able to overcome by an effort of convergence. The singular feature in the case was the simultaneous presence in the double image test of two modes of localization of biretinal stimuli, a condition which is akin to binocular triplopia. There was no actual monocular diplopia, but the phenomenon demonstrated may be considered as a precursor to binocular triplopia.

W. Zentmayer.

Operations

Restoration of the Lower Cul-de-Sac. C. Berens, Am. J. Ophth. 26: 119 (Feb.) 1943.

Berens gives the following summary:

"In five patients, whose inferior culs-de-sac were obliterated by scar tissue, resulting in ectropion, the orbital scar tissue was excised and the conjunctiva undermined over the lower half of the cul-de-sac. Incision was made to the lower margin of the orbit. Three double-armed sutures were passed through the conjunctiva and lower eyelid to attach the conjunctiva to the inferior orbital margin. A good inferior cul-de-sac was formed in each case and a prosthesis could be worn with satisfaction."

W. S. Reese.

Parasites

Ophthalmoscopic Observation of Microfilarias in the Vitreous of Patients Infected with Onchocerciasis. A. T. Estrada, Am. J. Ophth. 25: 1445 (Dec.) 1942.

Estrada reached the following conclusions:

It is possible to observe the microfilarias in the vitreous with the electric direct image ophthalmoscope.

The microfilarias seem to be more abundant in the vitreous than in the anterior chamber.

Observation of the parasite is easier with the ophthalmoscope than with the slit lamp microscope. The organism may be seen with the ophthalmoscope in cases in which nothing is seen in the anterior chamber, and even in those in which biopsy specimens of the skin are negative for the parasite.

The examination is so easy that it can be made by general practitioners and by visiting nurses connected with sanitary missions in the infected areas.

Microfilarias can be observed in the vitreous at early stages in the development of the disease.

W. S. Reese.

Pharmacology

Ophthalmic Ointments. L. M. Scheineson, Am. J. Ophth. 26: 171 (Feb.) 1943.

Scheineson gives the following summary:

"1. Ophthalmic ointments in general are advantageous for certain types of drug application.

"2. Certain types of ophthalmic ointments are best for certain conditions.

"3. For ophthalmic use water-absorption bases are superior to other bases.

"4. These ointment bases have a low surface tension.

"5. Ophthalmic ointments should be buffered.

"6. The specific method for preparing several types of ophthalmo-therapeutic ointments is given in detail." W. S. REESE.

Refraction and Accommodation

THE GREAT USEFULNESS OF BICYLINDRIC COMBINATIONS IN THE EXPLORATION OF ASTIGMATISM. M. MARQUEZ, Am. J. Ophth. **25:** 1458 (Dec.) 1942.

Marquez gives the following summary:

"There is a skillful process of investigating, chiefly the small degrees of astigmatism, based on the unquestionable existence of biastigmatism, and consisting in the employment of every kind of bicylindric combination. The first cylinder corrects the corneal astigmatism according to ophthalmometric measures (by Javal-Schiøtz or another keratometer). The second cylinder is searched for (after the corneal astigmatism has been corrected, and, if necessary, the spheric refraction) by the clock dial, as in the usual process of subjective exploration of astigmatism until the intensity of all diameters is equalized. Once having found the two cylinders, the resultant single cylinder is obtainable (with or without a spheric fraction) by means of formulas, graphs (both processes having been described in the text of this paper), or tables. This bicylindric process has a sensitiveness much greater than that of Jackson's cross-cylinder test (which is only a special variety of the former) or any other subjective process for exploring astigmatism." W. S. REESE.

THE EFFECT OF UNDERCORRECTION AND BASE-IN PRISM UPON THE MYOPIC REFRACTIVE STATE. J. CHANCE, E. OGDEN and K. B. STODDARD, Am. J. Ophth. **25:** 1471 (Dec.) 1942.

From their studies the authors conclude that undercorrection of myopia and the wearing of base-in prisms have little, if any, tendency to reduce myopia unless the defect is pseudomyopia.

W. S. REESE.

Trachoma

STUDIES ON THE INFECTIVITY OF TRACHOMA. L. A. JULIANELLE, Am. J. Ophth. **26:** 280 (March) 1943.

Julianelle gives the following summary of his investigations:

"Human conjunctival cells containing demonstrable trachomatous virus have been grafted successfully upon the chorioallantois of the developing chick embryo. Proliferation of the epithelial cells was not accompanied by multiplication of the virus itself, as judged by animal inoculation and microscopic examination. Direct injections of macerated infective tissues into the yolk similarly failed to support detectable propagation of the virus. As possible explanations for this failure are offered the exalted specialization of the virus and its prolonged period of lag."

W. S. REESE.

Tumors

PRIMARY SARCOMA OF THE CHOROID. A. BARLOW, Am. J. Ophth. **25:** 1337 (Nov.) 1942.

Barlow reports a case of sarcoma of the choroid in a woman aged 32. The eye was enucleated twelve years later, after iridectomy for glaucoma, and the patient died seven years later of cerebral thrombosis. There was no clinical or postmortem evidence of metastasis.

W. S. REESE.

MULTIPLE PRIMARY MALIGNANT NEOPLASM. M. K. ASBURY and D. VAIL, Am. J. Ophth. **26:** 688 (July) 1943.

The authors report a case of multiple malignant neoplasms, one an intraocular malignant melanoma of the choroid, and the other, which was the cause of death, a glioblastoma multiforme of the cerebrum. The neoplasm of the choroid was seen to develop from a nevus which had been under observation for three years before it began to increase in size.

The article is illustrated. W. ZENTMAYER.

Uvea

CHOROIDEREMIA. R. G. SCOBEE, Am. J. Ophth. **26:** 1135 (Nov.) 1943.

Scobee agrees with Bedell that choroideremia is postnatal pathologic dissolution, and not congenital absence of the choroid. He gives the following summary:

"Two typical cases of choroideremia, one in an early and the other in a late stage, are reported in brothers aged 18 and 24 years, who lacked a hereditary background for the condition. Both have remarkably good vision in view of the fundus changes present; one is myopic, the other hypermetropic. Choroid and retina are present only at the extreme periphery and at the macula in all fundi. Their fundus reflex is greenish-white in color. Bilateral annular scotomata are present in both cases, night blindness only in the more advanced one. The more advanced case has innumerable tiny pigment balls fixed to the vitreous framework, and the anterior vitreous fibrils appear striated; degenerative changes could be observed in the vitreous picture in 30 days' time. Both patients have an early bilateral nerve-type deafness. The vitreous findings in addition to the audiographic examination would seem to furnish further evidence that choroideremia is a degenerative process primarily and not a congenital defect. W. S. REESE.

Vision

THE TREATMENT OF AMBLYOPIA. F. B. FRALICK, Am. J. Ophth. 26: 1195 (Nov.) 1943.

Fralick gives the following summary:

"The early recognition and treatment of amblyopia offers the greatest percentage of successful results. The entire field of orthoptic treatment is opened up for subsequent exploitation only through its successful correction. Those individuals obtaining and retaining acceptable industrial vision have a tremendous economic advantage. No amblyopic eye should be considered due to a congenital defect until all forms of occlusion therapy have been used continuously and totally for a period of several months without demonstrable visual improvement."

W. S. REESE.

Therapeutics

THE PRODUCTION AND TREATMENT OF EXPERIMENTAL PNEUMOCOCCAL HYPOPYON ULCERS IN THE RABBIT. J. M. ROBSON and G. I. SCOTT, Brit. J. Exper. Path. 24: 50 (April) 1943.

A comparatively well standardized ulceration of the rabbit cornea, frequently accompanied by hypopyon, was produced by the intracorneal injection of Diplococcus pneumoniae type 19. The therapeutic effects of sodium penicillin (650 Oxford units per cubic centimeter), sodium sulfacetimide (30 per cent solution), sodium sulfapyridine (30 per cent solution) and tyrothricin (1 milligram per cubic centimeter) were studied. The antibacterial agents were instilled at various intervals for thirty-six hours. Thereafter the solutions were applied hourly during the day. Treatment was not continued beyond the fifth day.

The best results were achieved with the penicillin therapy. Even when treatment started twenty-four hours after inoculation, it was of some value. Sodium sulfacetimide had little effect when six hours had elapsed between inoculation and treatment but was highly beneficial in prevention of the ulceration when applied earlier.

The experiments with sodium sulfapyridine were discontinued after one series because of the conjunctival irritation after repeated instillations of the alkaline solution and because ulcerations could not be prevented even when treatment began one hour after inoculation. Tyrothricin was of possible slight benefit when treatment was started one hour after injection, but ulcers developed in all treated eyes.

L. VON SALLMANN.

Society Transactions

EDITED BY DR. W. L. BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

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Feb. 21, 1944

Lateral Proboscis with Cyclopean Eye: Further Report on a Case. DR. LOUISE H. MEEKER and DR. RUDOLPH AEBLI.

This paper will be published in full in a later issue of the ARCHIVES.

Intrinsic Variability of Astigmatic Errors. DR. JOSEPH I. PASCAL.

This paper will be published in full in a later issue of the ARCHIVES.

Differential Diagnosis of Paresis of the Right Superior Oblique Muscle and the Left Superior Rectus Muscle. DR. W. THORNWALL DAVIS, Washington, D. C.

This paper will be published in full, with discussion, in a later issue of the ARCHIVES.

Effects of High Altitude Flying and Deep Sea Diving on Ocular Function. CAPTAIN LEON D. CARSON (MC), U. S. N.

This paper will be published in full, with discussion, in a later issue of the ARCHIVES.

Book Reviews

Archivos de la Asociación para evitar la ceguera en México. Vol. I. Dr. L. Sánchez Bulnes, Editor in Chief. Pp. 173.

This, the first volume of the *Annals of the Mexican Society for the Prevention of Blindness,* has just appeared. After an introductory note by Dr. Baz, minister of public welfare, a history of the association is given by Dr. C. R. Margain. At a meeting of the section on ophthalmology of the National Medical Congress in 1918, Dr. J. de J. González urged the formation of the society, and it was legally incorporated in 1922. Originally supported by voluntary contributions, it was aided by a grant from President Calles in 1924 and grew from a small office for free consultations to the present hospital, which was opened in 1939, under the direction of Dr. L. Sánchez Bulnes. Further grants, amounting to more than $100,000, were made by the government in 1941. The endowment of the association, aside from its building, now amounts to some $125,000.

A statistical analysis of the work of the association in 1942 is presented by Drs. Daniel and Fernando Silva. The number of patients cared for was 13,410. In all, 24,507 treatments were given, 2,072 refractions carried out, 135 photographic studies of the external portion of the eye or the fundus made and 437 operations performed. Of the operations, 261 were performed on ambulatory patients, including 81 operations for pterygium. One hundred and eighty-six operations, including 112 extractions of cataracts, required hospitalization. The small number of operations for glaucoma (10) and for muscular anomalies (17) is noteworthy. Patients make voluntary donations for the services rendered according to their means, and these gifts, with the collections for glasses and drugs, amounted to $18,987, against the total of $30,599 expended, during the year. Twenty-five per cent of patients were unable to make any donations.

The ambulance service is described by Dr. J. Sáenz Canales. By means of a well fitted ambulance dispensary, with a staff of two doctors and a nurse, forty-five towns and villages outside the federal district were visited. Lectures on the care of the eyes and the prevention of blindness were given in schools and at public meetings of various sorts. Aid was given to local health officers in prophylaxis against ophthalmia neonatorum, and vials for the Credé treatment were dispensed. Consultations were held in various towns with the local general practitioners, who were advised as to the care of patients with simple conditions and were furnished with the necessary drugs. Refractions were carried out, the prescriptions being filled at the central hospital. Some minor operations were performed in the ambulance, while patients requiring hospitalization were sent to the central hospital, where treatment or operation was provided without cost. From 200 to 900 patients per month were seen by this ambulance team.

The scientific and clinical contributions included in the volume are as follows: "Retrocorneal Hyaline Trabeculae Following Interstitial Keratitis," by L. Sánchez Bulnes; "Cysts of the Vitreous," by J. Sánchez Canales; "Ocular Biomicrophotography," by M. de Rivas Cherif; "The Problem of Pupillary Occlusion," by H. Fernández Isassi; "An Intraocular Foreign Body," by R. Olivera López; "The Suture in Cataract Extraction," by Luis E. Martinez, and "A Case of Marcus Gunn's Phenomenon," by V. Ramírez Esteva.

It is planned to publish two numbers of the *Archivos* each year. The association is to be congratulated on the appearance and content of the volume, and especially on its record of remarkable achievement against many obstacles.

SANFORD R. GIFFORD, M.D.

A New Conception of Keratoconjunctivitis Sicca. By Henrik Sjögren, Jönköping, Sweden. English translation by Dr. J. Bruce Hamilton, Hobart, Tasmania. Pp. 152, with 56 illustrations. Price, 25 shillings. Glebe, Sydney, Australia: Australasian Medical Publishing Company, Ltd., 1943.

Dr. Hamilton's translation of Dr. Henrik Sjögren's monograph on keratoconjunctivitis sicca makes this important article now available to English readers. In a foreword are listed additional articles on this subject by the author and by others which have appeared since the publication of the monograph, in 1933; these articles have added little to knowledge of this syndrome. Dr. Hamilton believes that there are still several problems concerned with this subject which are open for investigation. These concern the pathologic picture of the arthritic condition; the blood count and sedimentation rate, which should be determined periodically; the bacterial content of the purulent salivary secretion; a quantitative analysis of the salivary secretion; a possible reaction to atrophic rhinitis and, finally, the relation of idiopathic corneal ulcer and diminished lacrimal secretion. At the end of the monograph, Dr. Hamilton has added an appendix dealing with treatment, about which nothing is said in the original article. Treatment,

which consists in occlusion of the canaliculi by electrocoagulation, has given good results in the hands of Beetham and Rucker. The preparation and instillation of artificial tears are described.

Dr. Hamilton tentatively concludes that there are two forms of keratitis sicca: The first, a true desiccation of the cornea with erosions, with or without filaments, is the more common and responds to electrocautery. The second, in which there is intermittent vesicular keratitis with attacks of arthritis or parotitis, responds only partially to such treatment. At the same time, treatment of the other manifestations of this symptom complex will not be satisfactory, since the etiologic factors require further research. The work of the translator has been well done, and the printing and the illustrations are clear and distinct. The abstracter draws attention to two recent articles which give an excellent review of this interesting topic (Bruce, G. M.: Keratoconjunctivitis Sicca, Arch Ophth. **26:** 945 [Dec.] 1941. Gifford, S. R.; Puntenney, I., and Bellows, J.: Keratoconjunctivitis Sicca, ibid. **30:** 207 [Aug.] 1943).

Arnold Knapp.

Education and Health of the Partially Seeing Child. By Winifred Hathaway. Price, $2.50. Pp. 216. Published for the National Society for the Prevention of Blindness, Inc. New York: Columbia University Press, 1943.

The well known organization which has rendered a public service in pointing out and forestalling visual hazards widens still further the field of its activities. Recognizing the social and economic problem presented by a large number of visually handicapped children of school age, it has sponsored the present comprehensive and constructive survey. As its title indicates, this book deals with the health, as well as the education, of the partially seeing child. Intended for teachers, nurses, social service workers and others concerned with the welfare of the young, the material has been gathered from various sources in education, both lay and medical, and from industry, engineering and public health.

After reviewing the history of endeavor in this field, both here and abroad, the administrative responsibilities of classification, program planning and selection and training of teachers, Miss Hathaway discusses in detail the basic principles and technics of sight saving. These include the curriculum; the teaching of tool subjects, such as large type material (of which there is an unfortunate shortage), typewriting, chalk board writing, motivated art and hand work, as well as mechanical devices, such as recording machines, talking books and the radio. A special chapter is devoted to child guidance, individual and collective, in community social service and by civic organizations.

Among a number of appendixes, there is a useful one on the checking of lighting facilities and the installation of and equipment for ophthalmic work in the classroom.

The laudable character of this helpful undertaking and the excellent presentation of so important a subject are worthy of all praise and seem to disarm any but the most favorable criticism. However, from a sociologic standpoint, there are some misgivings as to the advisability, in many cases, of the undertaking of an education which is beyond the handicapped child's capacity, such as sending him to college and later, perhaps, to a professional school. Hopes may be aroused only to be met with frustration by inadequacies which are realized too late, and thus the original feeling of inferiority inherent in the visual handicap may be increased. As if this objection had been anticipated—if not foreseen—the psychologic, as well as the practical, approach to this serious problem is considered at length in a special chapter on prevocational and vocational guidance and training. In a well prepared and inspiring blueprint for the future of this service, entitled "The Road Ahead," the author has reviewed the results already accomplished by various agencies—medical and surgical, educational, socioeconomic and industrial—which have engaged in measures for sight saving in the widest sense, including that of community responsibility. The author appeals for even more extensive and active participation and cooperation in this campaign.

Percy Fridenberg.

Directory of Ophthalmologic Societies*

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

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Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

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Place: Rosario. Time: Last Saturday of every month, April to November, inclusive. All correspondence should be addressed to the President.

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CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Paul A. Chandler, 5 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. L. L. McCoy, 1317 Marion St., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. H. Pike, Midland, Mich.
Secretary-Treasurer: Dr. R. H. Criswell, 407 Phoenix Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Ray Parker, 218 Franklin St., Johnston, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. C. A. Ringle, 912-9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer:: Dr. C. K. McLaughlin, 567 Walnut St., Macon.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. J. K. Von Lackum, 117-3d St. S. E. Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St Des Moines.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Val H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. McGeary, 920 Medical Art Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St St. Paul.
Time: Second Friday of each month from October t May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings, Mont.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St.. Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr B. E. Failing, 31 Lincoln Park, Newark.
Secretary: Dr. George Meyer, 410 Haddon Ave., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. James E. McAskill, 508 Woolworth Bldg., Watertown.
Secretary: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. T. W. Buckingham, 405 Broadway, Bismarck.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. R. B. Maw, 699 E. South Temple, Salt Lake City.
Secretary-Treasurer: Dr. Charles Ruggeri Jr., 1120 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. William B. Agan, 1 Nevins St., Brooklyn.

Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn.

Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. Walter F. King, 519 Delaware Ave., Buffalo.

Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.

Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.

Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.

Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.

Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago.

Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.

Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.

Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman: Dr. Shandor Monson, 1621 Euclid Ave., Cleveland.

Secretary: Dr. Carl Ellenberger, 14805 Detroit Ave., Cleveland.

Time: Second Tuesday in October, December, February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.

Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.

Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. H. D. Emswiler, 370 E. Town St., Columbus, Ohio.

Secretary-Treasurer: Dr. D. G. Sanor, 206 E. State St., Columbus, Ohio.

Place: The Neil House. Time: 6 p. m., first Monday of each month.

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Arthur Padillo, 414 Medical Professional Bldg., Corpus Christi, Texas.

Secretary: Dr. Edgar G. Mathis, 815 Medical Arts Bldg., Corpus Christi, Texas.

Time: Second Friday of each month from October to May.

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Abell Hardin, Medical Arts Bldg., Dallas, Texas.

Secretary: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas, Texas.

Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.

Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.

Time: 7:45 p. m., third Monday of every month from September to May.

DETROIT OPHTHALMOLOGICAL CLUB

Chairman: Dr. Howell L. Begle, 2730 E. Jefferson Ave., Detroit.

Secretary: Dr. C. W. Lepard, 1025 David Whitney Bldg., Detroit.

Time: 6:30 p. m., first Wednesday of each month, November through April.

DETROIT OPHTHALMOLOGICAL SOCIETY

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.

Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.

Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President: Appointed at each meeting.

Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.

Time: Third Wednesday in October, November, March, April, May and June.

EASTERN PENNSYLVANIA ASSOCIATION OF EYE, EAR, NOSE AND THROAT PHYSICIANS

President: Dr. James E. Landis, 232 N. 6th St., Reading.

Secretary-Treasurer pro tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.

Time: Last week in April each year.

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.

Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.

Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SECTION

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.

Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.

Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

INDIANAPOLIS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.

Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.

Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.

Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.

Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.

Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.

Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. E. Trainor, 523 W. 6th St., Los Angeles.

Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

LOUISVILLE EYE AND EAR SOCIETY

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time. 6:30 p. m., second Thursday of each month from September to May, inclusive.

LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Each member in alphabetical order.

Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Each member in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave, Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. Edwin C. Bach, 324 E. Wisconsin Ave., Milwaukee.

Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.

Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.

Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.

Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

MONTREAL OPHTHALMOLOGICAL SOCIETY

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.

Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.

Time: Second Thursday of October, December, February and April.

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.

Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashvile, Tenn.

Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May

NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.

Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

NEW ORLEANS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.

Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.

Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Frank C. Keil, 660 Madison Ave., New York.
Secretary: Dr. Willis S. Knighton, 121 E. 61st St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Sigmund Agatston, 875–5th Ave., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.
Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. D. D. Stonecypher, Nebraska City, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.
Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. John B. McMurray, 6 S. Main St., Washington, Pa.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. R. M. Brickbauer, Shillington, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. C. C. Beisbarth, 3720 Washington Blvd., St. Louis.
Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.
Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. E. W. Campbell, 316 Michigan St., Toledo, Ohio.
Secretary: Dr. L. C. Ravin, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. S. Bockoven, 1752 Massachusetts Ave., Washington, D. C.
Secretary-Treasurer: Dr. John Lloyd, 1218–16th St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.

ARCHIVES OF OPHTHALMOLOGY

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INTRACAPSULAR CATARACT EXTRACTION

STATISTICAL SURVEY OF FIVE HUNDRED CONSECUTIVE CASES

FREDERICK ALLISON DAVIS, M.D

MADISON, WIS.

In this report is submitted a statistical analysis of the records of 500 consecutive cases of intracapsular extraction performed by me and my associates on the staff of the University of Wisconsin General Hospital up to December 1940. I reported 200 of these cases before the American Academy of Ophthalmology and Otolaryngology in 1937.[1] The data concerning these two series of intracapsular operations, 200 in the first and 300 in the second, have been combined here in order to present a more comprehensive survey of our results.

A full discussion of the operative technic employed, namely, the forceps expression method, together with the preoperative and postoperative care of the patient, was given in the previous paper and will not be repeated here. This report, therefore, will be limited in this respect to such additional information as has been gleaned from experience in the second series of 300 cases. Since these data were first compiled, my colleagues and I have performed about 400 additional intracapsular extractions, but a detailed analysis of the case reports of this series has not yet been made. At the outset, I may state that we have retained the same technic as that originally described, with only minor variations.

Experience in a series of operations now approaching 1,000 has served to reenforce our conviction of the soundness of the intracapsular method of cataract extraction, and in my opinion it should be the operation of choice in most cases of senile cataract.

STATISTICAL ANALYSIS OF FIVE HUNDRED CASES OF INTRACAPSULAR EXTRACTION

The ages of the patients are shown in table 1, in which the cases are grouped according to age decades, from 30 to 90 years. The youngest patient to be operated on was 33 and the oldest 87 years of age.

The state of maturity of the cataracts is shown in table 2, 272 being classified as mature, 173 as immature and 55 as hypermature.

ETIOLOGIC FACTORS AND ASSOCIATED DISEASES

The primary cause of the cataract could not be determined in most instances. Diabetes was present, in various stages, in 39 cases; in 17 of these cases diabetic retinitis was a complication. The diabetes appeared to be the primary cause of the cataract in only a limited number of cases.

In 7 cases there was high myopia. In such cases operation is usually performed by the extracapsular method, but because of the immaturity

TABLE 1.—*Ages of Five Hundred Patients Subjected to Intracapsular Cataract Extraction*

Age, Years	No. of Cases
30 to 40	2
40 to 50	27
50 to 60	79
60 to 70	166
70 to 80	194
80 to 90	32
	500
Sex	
Males	275
Females	225
	500

TABLE 2.—*Description of Cataracts*

Type of Cataract	No. of Cases
Mature	
Sclerosed	80
Ordinary senile (cortical)	192
	272
Immature	
Amber nucleus, clear cortex	115
Ordinary cortical, including postsubcapsular and intumescent	58
	173
Hypermature	
Shrunken	20
Fluid cortex; rubbery capsule	26
Soft cortex	2
Sclerosed	7
	55
Grand total	500

Read at a meeting of the Chicago Ophthalmological Society, May 19, 1941.

From the Department of Ophthalmology, University of Wisconsin Medical School.

1. Davis, F. A.: Personal Experiences with Intracapsular Cataract Extractions, Tr. Am. Acad. Ophth. **42**:218, 1937; Arch. Ophth. **19**:867 (June) 1938.

of the cataract the intracapsular procedure was employed. There was no loss of vitreous in any of these cases.

Chronic simple glaucoma was present in 12 cases. In 3 cases a previous trephining or a modified Lagrange procedure, with inclusion of the iris, was done. A small bead of vitreous was lost in 1 of these cases, that of a patient aged 81, when the iris pillar was replaced. No vitreous was lost in the other 11 cases. In all cases the glaucoma had been brought under control by treatment, no patient having high intraocular tension at the time of operation. In 2 cases the tension was very low, with deep glaucomatous cupping. The designation of the condition as glaucoma in these 2 cases of course is questionable.

In 2 cases cataract of allergic origin was associated with severe and extensive dermatitis venenata, of long standing. One patient had had a detachment of the retina for eight years or longer. In a number of cases there was subluxation of the lens, the condition being congenital in some cases and the lens being hypermature and shrunken in others, with vitreous in the anterior chamber. Other, rarer, types which were encountered and the associated lesions are shown in table 9.

TABLE 3.—*Method of Operation*

	No. of Cases
Preliminary iridectomy	223
Extraction combined with iridectomy	246
Simple extraction	
Without iridectomy	3
Peripheral iridectomy	28
Total	500

In table 3 are recorded the methods of operation employed. Iridectomy of some type was performed in practically every case in this series.

I personally prefer, and generally use, extraction combined with complete or peripheral iridectomy. Simple extraction, when uncomplicated by incarceration or prolapse, produces the ideal postoperative result, but, as I have previously pointed out, from the standpoint of safety and ease of extraction complete iridectomy has a distinct advantage. With some of the younger subjects, with healthy, active irises, for whom a perfect cosmetic result is desirable, we employ simple extraction with peripheral buttonhole iridectomy. However, it cannot be denied that extraction undeniably is more difficult through the round pupil, especially when, as is not infrequently the case, the pupil cannot be dilated sufficiently to permit easy passage of the lens.

In most of the 31 cases in which the lens was extracted through the round pupil, the subjects were young. In all cases the method was successful from an operative and a visual standpoint, but postoperative prolapse of the iris beneath the conjunctival flap, requiring excision, developed in 3 cases. This complication is serious and, in my opinion, should be avoided at all costs. It is especially important that it be avoided in older, feeble and uncooperative subjects.

In table 4 is recorded the condition of the capsule on delivery of the lens. In 424 (84.8 per cent) of the cases the capsule was intact (+), and in 76 (15.2 per cent) it was broken (±).

TABLE 4.—*Condition of Capsule on Delivery of Lens*

	No. of Cases	Percentage
Capsule intact (+)	424	84.8
Lens and capsule (capsule was ruptured during or after passage through wound but was completely removed (±)	76	15.2
Total	500	

At times a portion of the capsule of the lens may become caught in the wound if it ruptures during delivery. The incarcerated portion can frequently be pulled out by reintroduction of the smooth forceps just inside the lips of the wound. In the cases in which we failed to deliver the lens with the capsule the operation was classified as "attempted intracapsular extraction." These cases are not included in this survey, since extracapsular extractions were done. They numbered 105, or 17.4 per cent, of a total of 605 operations. Thus, intracapsular delivery was successful in 82.6 per cent of the entire series in which it was attempted.

TABLE 5.—*Tabulation of Successful and Unsuccessful Intracapsular Deliveries*

		Number	Percentage
Total number of intracapsular operations attempted		605	
Delivery in capsule	500		82.6
Extracapsular delivery	105		17.4
First series: operations attempted		252	
Delivery in capsule	200		79
Extracapsular delivery	52		21
Second series: operations attempted		353	
Delivery in capsule	300		85
Extracapsular delivery	53		15

In table 5 the successful and unsuccessful deliveries are shown separately, as well as combined. It will be noted that in the first series 200, or 79 per cent, of the cataracts were delivered in capsule, while in the second series 300, or 85 per cent, were delivered in capsule.

Our experience with rupture of the capsule is similar to that previously reported. It is most common with the intumescent, slightly swollen lens with a tense capsule. In our first series

we had more failures with the large, hard, brown, sclerosed type of lens in which no soft cortex was present. Such a lens will not mold, since it consists of a hard nucleus only. In the second series we have been somewhat more successful with this type, since we avoid taking too large a bite or grasp of the capsule and thereby prevent its rupture. More emphasis is placed on exertion of pressure with the spoon, and thereby we have had fewer ruptures of the capsule in extracting this type of cataract. The capsule may be noted to be torn between the jaws of the forceps after the lens has been delivered; but if one avoids releasing or regrasping the capsule, successful intracapsular delivery can frequently be accomplished in spite of this.

The hypermature lens with fluid cortex and distended, taut, rubbery capsule still presents a problem for removal by the intracapsular method, since it is impossible to grasp the capsule. There were 26 cases of this type, as will be noted in table 2. In 11 of these cases we removed the cataract successfully by the Smith method, with external pressure alone, without benefit of forceps. Vitreous was lost in but 1 of these cases, and then only a drop, with final vision of 20/20. Application of external pressure alone is also at times successful in delivery of the intumescent lens if the age of the patient is sufficiently advanced, and it should be attempted if the capsule cannot be easily grasped.

The immature lens, with a central nuclear haze, clear periphery and soft, pultaceous, clear cortex, is the ideal type for intracapsular extraction. The capsule moves freely on the underlying cortex. It is thus easily grasped without rupture, and delivery in the intact capsule is successful in almost 100 per cent of cases.

As was noted in my previous communication, the operation is most successful in persons of the age group from 60 to 90 years, since the zonule appears weakened and breaks easily. However, my associates and I have grown much less apprehensive concerning delivery in capsule in persons of the younger age group, from 40 to 50. As was previously pointed out, the soft, white, rapidly developing cataract in younger subjects has frequently proved surprisingly easy to deliver. This second series, of 300 operations, has confirmed my previous experience in this regard. Intracapsular extraction in young subjects, under 40 years of age, is usually not successful, especially when the cataract is immature and partly clear or is of the congenital or juvenile type, since the zonule is tough and elastic and will not rupture easily. Cataracts of allergic origin and those which develop from dinitrophenol poisoning cannot usually be delivered in capsule in subjects under 50 years of age.

In any case, if the zonule does not break readily with moderate pressure on the globe, we usually abandon the effort and remove the capsule with the Fuchs capsule forceps.

PROLAPSE OF THE VITREOUS

In table 6 are indicated the cases in which vitreous was lost in any amount whatever, the amount recorded in the description of the operation, the time of the loss and the final vision obtained. I make a practice of recording "vitreous lost" in any case in which the hyaloid membrane ruptures, as evidenced by sudden deepening of the chamber, and in any case in which the slightest film of vitreous is noted on the spatula, even though no measurable quantity is lost. As will be noted, there was loss of vitreous in 36 cases, or 7.2 per cent of the 500 cases of

TABLE 6.—*Summary of Data in Cases in Which Vitreous Was Lost* *

Operative Record of Amount Lost	No. of Cases
Tiny bead to 1 drop	16
Two to 3 drops	7
Four drops	4
Moderate loss	5
Eight drops	1
Vitreous flowed out (liquid)	3
	36

Fluid vitreous noted in 7 cases

Time of Loss of Vitreous	No. of Cases
After section	7
During delivery	4
After delivery of lens	19
On replacement of pillar	6
	36

Vision	No. of Cases
20/15	4
20/20	12
20/30	9
20/40	2
20/50	1
20/70	1
20/100	1
20/200	4
Light perception	1
Unknown	1
	36

* The total of 36 cases represents 7.2 per cent of the 500 cases in which this operation was performed. The capsule was intact in 34 cases and broken in 2 cases.

intracapsular extraction. The 10 cases in which vision was less than 20/30 will be discussed more fully later. The incidence of loss of vitreous was only 6 per cent in the first series, of 200 cases. The increase in the second series is probably due to the fact that the selection is now less careful than in the first series and, also, that all members of the staff, including house officers, are now using the intracapsular method.

Our incidence of loss of vitreous was lower after intracapsular extraction than after extracapsular extraction, at least in a small series of 100 cases of the latter operation performed during the period of our first series of 200 intracapsular operations, in 9 per cent of which there was loss of vitreous. Gradle,[2] Gailey[3] and others have

2. Gradle, H. G.: Intracapsular Versus Extracapsular Extraction of Cataract, Tr. Sect. Ophth., A. M. A., 1933, p. 186.

3. Gailey, W. W.: A Report on Two Hundred Cataract Operations, Illinois M. J. **72:**528 (Dec.) 1937.

reported similar experiences, while Berens and Bogart,[4] in a recent review of 1,004 operations, reported that the incidence of loss of vitreous was about the same with the two methods, namely, 9.9 per cent for the intracapsular and 9 per cent for the extracapsular procedure. Knapp,[5] in his series of 500 cases, reported loss of vitreous in 8.4 per cent; Greenwood and Grossman,[6] in a series at the Massachusetts Eye and Ear Infirmary, in 6.2 per cent, and Bothman,[7] in a series in India, in 4.5 per cent.

In table 7 are recorded the data in the 11 cases in which there was loss of vitreous and vision was less than 20/30. In all but 4 of these cases the lowered visual acuity appeared to be due to previous disease, such as diabetic retinopathy (cases 5 and 6), old chorioretinitis (case 8), macular hemorrhage due to hypertensive retinopathy (case 3), chronic simple glaucoma (case 1), amblyopia ex anopsia associated with a subluxated lens of fifteen years' duration (case 9) and iritis of long standing with synechiae (case 10). In case 2 a drop of vitreous was lost. The healing was prompt, the patient being discharged on the fourteenth postoperative day. This patient did not return for final refraction.

Table 7.—*Analysis of Cases with Loss of Vitreous and Vision of Less than 20/30*

Case No.	Description	Vision	Capsule
1	Bead on replacement of pillar (C. S. G.*)	20/40	Broken
2	One drop after delivery (vision on 14th day)	20/40	Intact
3	Three drops after delivery (hypertensive retinopathy; macular hemorrhage)	20/50	Intact
4	Three drops (fluid vitreous)	20/70	Intact
5	One drop after delivery (diabetic circinate retinopathy, both eyes; macular lesions)	20/100	Intact
6	One drop after delivery (diabetic retinopathy; macular lesions in both eyes)	20/200	Intact
7	Four drops (vision 20/30 on discharge); late iritis, with reduction of vision to	20/200	Intact
8	Moderate loss (fluid; complicated cataract; old central chorioretinitis; absolute glaucoma in other eye)	20/200	Intact
9	Tiniest amount (subluxated lens 15 years; lens lifted out with forceps; amblyopia ex anopsia)	20/200	Intact
10	Light perception; complicated cataract synechiae; secondary glaucoma in both eyes	Light	Intact
11	Four drops with section	Unknown	Intact

* C. S. G. indicates chronic simple glaucoma.

Credit for the notable reduction in the incidence of loss of vitreous in cases of intracapsular extraction undoubtedly belongs to Van Lint, who introduced the use of akinesia. Certainly, the amount of vitreous lost has been materially lessened by the elimination of the possibility of the patient's squeezing the eye. Solution of tribromoethanol U. S. P. was used in 10 per cent of this series of operations. We still use it in operations on highly nervous, unruly or ignorant subjects, especially when the eye is extremely prominent or the tension elevated. With added experience we have had no occasion to change the conclusions which I expressed in a communication on this subject several years ago.[8] My colleagues and I are now using pentothal sodium in selected cases, but our series is not sufficiently large to justify a report on the results at this time.

In table 8 are recorded the cases of incarceration and prolapse of the iris. Prolapse occurred in 7 cases, in 3 after simple extractions; in 2 of these cases the complication was apparently brought on or aggravated by postoperative vomiting. Excision of the prolapsed iris was usually made as soon as it was discovered. Case 6 is of interest because of the profound coma which developed on the operating table, the coma apparently being due to an idiosyncrasy or an unusual response to pentobarbital sodium, which was given prior to operation. A dose of 1½ grains (0.097 Gm.) was administered by mouth fifteen minutes prior to operation. The patient remained irrational throughout the night and was uncontrollable. Prolapse of the iris under the flap, and probably loss of vitreous, may have occurred, although the conjunctival flap was not disturbed and the sutures were in place. In case 7 severe hyphemia with prolapse followed a blow on the eye. In case 8 there was a simple incarceration of one pillar, with no visible prolapse. Healing was

Table 8.—*Incarceration and Prolapse of the Iris*

Case No.		Visual Acuity
1	Prolapse, second day; simple extraction; vomiting	20/20
2	Prolapse, second day; simple extraction; vomiting	20/20
3	Prolapse, second day; simple extraction; hyphemia	20/30
4	Prolapse, eleventh day; one pillar; overactivity at home	20/20
5	Prolapse, one pillar; patient struck eye	20/40
6	Prolapse, one pillar; patient comatose on table; irrational; "hammock pupil"	20/50
7	Prolapse, one pillar; patient struck eye; wound sprung; hyphemia	H. M.*
8	Incarcerated pillar; secondary glaucoma	H. M.
	Adherent pillar, with no prolapse or complications, 21 cases	

* H. M. indicates hand movements.

4. Berens, C., and Bogart, D.: Certain Post-Operative Complications of Cataract Operations, Tr. Sect. Ophth., A. M. A., 1938, p. 238.

5. Knapp, A.: The Complications of the Forceps Intracapsular Cataract Operation Based on an Analysis of 500 Successive Cases, Tr. Am. Ophth. Soc. **34**:162, 1936.

6. Greenwood, A., and Grossman, H. P.: An Analysis of 1,343 Intracapsular Cataract Extractions by Forty-Eight Operators Following the Verhoeff Method, Tr. Am. Ophth. Soc. **33**:353, 1935.

7. Bothman, L.: Complications of Cataract Surgery in India, Illinois M. J. **62**:243, 1932.

8. Davis, F. A.: Tribromethanol (Tribromethyl-Alcohol, Avertin) as an Anesthetic in Eye Surgery, Tr. Am. Ophth. Soc. **29**:47, 1931.

prompt, with good vision, but secondary glaucoma developed, with pain and gradual deterioration of vision to perception of hand movements. Repeated operation failed to relieve the condition, and the eye was finally enucleated.

The records show an additional 21 cases in which one pillar was adherent to the line of incision. These cases presented no symptoms; the eyes healed promptly, and the visual acuity was not affected up to the time the records were reviewed. I always regard such cases with some concern, since an adherent pillar may be followed by a secondary rise in intraocular tension, as in case 8, previously cited. On the other hand, I have seen and followed for years many patients with this condition who showed no evidence of any complication.

HEMORRHAGE INTO THE ANTERIOR CHAMBER

Postoperative hemorrhage into the anterior chamber was noted in 46 cases (9.2 per cent), the time of occurrence ranging from the second to the seventeenth day. All of these hemorrhages, except in 5 instances, occurred from the second to the sixth postoperative day, and the great majority of them were on the fourth, fifth or sixth day. All were confined to the anterior chamber except in 3 cases, in which the vitreous was also invaded. In 12 cases they were due to trauma, but in a much larger number, 31 cases, hemorrhage seemed to occur spontaneously, without injury of any kind. In many cases the hemorrhages were small and cleared up promptly, but in a number the amount was considerable, the blood completely filling the anterior chamber and, in 3 cases, causing bulging of the flap, with external oozing. In a few cases bleeding was recurrent.

In my first series, of 200 cases, postoperative hyphemia occurred in 7 per cent; in the next 100 cases, in 9 per cent; in the fourth 100 cases, in 5 per cent, and in my most recent series, the fifth 100 cases, in 18 per cent. My average for the entire series, namely, 9.2 per cent, aproximates closely that given by other investigators (Wright,[9] 10 per cent; Vail,[10] 8 per cent, and Knapp,[11] in series of 100 cases reported in 1935, 9 per cent). However, Berens and Bogart[4] recorded only 4 per cent, while Bothman,[7] in an Indian series, reported 3.6 per cent.

9. Wright, R. E.: Lectures on Cataract: Posterior-Segment Complications in Post-Operative Period; Some Difficult Extractions, Am. J. Ophth. **20**:376 (April) 1937.

10. Vail, D. T., Jr.: On Hyphema After Cataract Extraction, Tr. Am. Ophth. Soc. **31**:496, 1933.

11. Knapp, A.: Intracapsular Operation for Cataract: Report on Fifth Hundred Successive Extractions, Arch. Ophth. **13**:823 (May) 1935.

In table 9 are summarized the data in all the instances of postoperative hemorrhage observed in the 500 cases, with notations as to the day on which the bleeding was first observed and the final visual acuity obtained.

As will be noted, in all but 8 of the 46 cases of postoperative bleeding final vision was 20/30 or better. In only 5 cases was the final visual acuity 20/70 or less. In 2 of these cases the patients were diabetic, vision in 1 instance being 20/200; the poor acuity in this case was entirely due to diabetic retinopathy, the blood being slight in amount and quickly absorbed. The patient whose final vision was limited to perception of hand movements struck the eye; the wound sprang; the iris prolapsed, and there was bleeding into both the vitreous and the anterior chamber. The patient whose vision was 20/100

Table 9.—*Data on Cases of Postoperative Hemorrhage into Anterior Chamber* *

Onset Day	No. of Cases	Vision	No. of Cases	Cause	No. of Cases
2d	3	20/15	13	Unknown	31
3d	3	20/20	14	Trauma	12
4th	8	20/30	8	Vomiting with prolapse of iris	1
5th	10	20/40	2	Prolapse of iris	1
6th	16	20/50	1	Polycythemia vera	1
7th	1	20/70	2		46
8th	1	20/100	1		
9th	1	20/200	1	Anterior chamber	43
10th	1	Hand movements	1	Anterior chamber and vitreous	3
11th	1		46		46
17th	1				
Unknown	1				
	46				

* The total of 46 cases represents 9.2 per cent of the 500 cases in which intracapsular extraction was performed.

was uncontrollable, twice pulling off the bandages, and on the eleventh day had a hemorrhage into the vitreous and the anterior chamber.

My study so far reveals no definite cause for the bleeding aside from postoperative trauma. Routine studies of the blood, including determination of coagulation and bleeding times, were made on practically all the patients. Special studies, including a platelet count, the tourniquet test and determinations of the vitamin C, prothrombin and calcium contents of the blood, were made on a large number of the patients, the results of which are to be reported later by my associate, Dr. E. E. Neff. A poor section, too far in the sclera, appears to predispose to postoperative hemorrhage. Two cases of hemorrhage were observed after simple extraction. In both these cases prolapse of the iris was caused by vomiting on the night of operation. Hyphemia is rare after a purely corneal section, as revealed by the Bothman series of 1,000 operations in India. Vail concluded that the bleeding is "the result of wound reopening and the rupture of newly formed corneo-episcleral blood vessels at

the section, and rarely from rupture or diapedesis from diseased iris vessels of inflammatory origin." He suggested the interesting theory, first advanced by von Grosz, that "increase of intraocular pressure and over-filling of the anterior chamber constitutes a 'crucial moment' when even the slightest lid pressure or ocular movement would be sufficient increment to cause the wound to reopen."

I am inclined to agree with this theory, since the time of bleeding in most cases is after the first dressing, when the wound is usually closed. Furthermore, on a few occasions bleeding has occurred at the exact moment of the first dressing. Therefore, in my opinion, the needless dressing of the eyes should be avoided and the first dressing postponed until the fourth day. Obviously, extreme care in all postoperative dressings is of the utmost importance, and undue pressure or manipulation of the lids should be avoided. Loss of vitreous does not appear to predispose to postoperative bleeding; in fact, the reverse seems to be true.

Postoperative bleeding is a most annoying complication, which, fortunately, rarely seriously affects the final result. The corneoscleral section, with the conjunctival flap, unquestionably predisposes to hemorrhage, since statistics reveal that bleeding is less common after a pure corneal section. However, I believe that most surgeons of the present day would be loath to give up the conjunctival flap and conjunctival sutures. Perhaps the deep corneoscleral suture, as advocated by Kalt,[12] Liegard,[13] Stallard,[14] Verhoeff,[15] McLean [16] and others, may prove to be the answer to the problem. I have used most of the various types of deep sutures but am not yet satisfied with any of them. Corneoscleral suturing is difficult and certainly complicates the operation. Sutures of the Kalt or the Stallard-Liegard type do not appeal to me, since they traumatize the cornea unduly and, further, fail accurately to approximate the edges of the wound. McLean's and Verhoeff's sutures produce a satisfactory closure, but their use is difficult in my hands. At present I place patches over both eyes for seven days, and so far this appears to have greatly reduced the number of cases of hyphemia. I believe that vigorous movements and squeezing of the fellow eye after removal of the patch may contribute to partial springing of the wound beneath the conjunctival flap of the eye operated on, with rupture of newly formed blood vessels. Suture of the deep wound might possibly avoid this, if the suturing was accurate and adequate.[17] However, I should be loath to abandon the conjunctival flap because of the safety it adds to the prevention of infection alone. Much of the criticism of the conjunctival suture is based on improper cutting of the flap, with the insertion of one suture, or not more than two, in a small pointed flap at the upper central part of the wound. I employ six to eight conjunctival sutures, placed in a flap which covers the entire incision, in most instances, from puncture to counterpuncture, so that the deep corneoscleral wound is completely covered. With this type of flap and method of suturing I have never seen the flap torn loose, with extrusion of vitreous, although slight separation of the edges of the deep wound is noted at times. This has apparently caused no trouble in most instances, the wound healing firmly after a few weeks.

TABLE 10.—*Visual Acuity in Five Hundred Cases in Which Intracapsular Extraction Was Performed*

Vision	No. of Cases		Percentage	Acuity
20/15	193			
20/20	153	413	82.6	20/30 or better
20/30	67			
20/40	19			
20/50	14			
20/70	11			
20/100	14	82	16.4	20/40 or less
20/200	13			
10/200-4/200	5			
Hand movements	4			
No vision	2			
Unknown	5		1.0	
	500			

RESULTING VISUAL ACUITY

Table 10 shows the record of visual acuity. Refraction is usually done six weeks after operation, when glasses are prescribed. However, in some instances the visual acuity recorded was the same as that noted after a brief refraction at the time of the patient's discharge, usually the

12. Kalt: Arch. d'opht. **21**:255, 1898; cited by Ellett, E. E.: Use of the Suture in Extraction of Cataract, Arch. Ophth. **17**:523 (March) 1937.

13. Liegard, cited by McLean, J. M., in discussion on Peter, L. C.: The Stallard Versus Multiple Conjunctival Sutures in Cataract Extraction, Tr. Am. Acad. Ophth. (1940) **45**:*46* (Jan.-Feb.) 1941.

14. Stallard, H. B.: A Corneo-Scleral Suture in Cataract Extraction: Its Technique and Advantages, Brit. J. Ophth. **22**:269 (May) 1938.

15. Verhoeff, F. H.: Corneo-Sclero-Conjunctival Suture in Operations for Cataract, Tr. Am. Ophth. Soc. **25**:48, 1927; Instrument for Simplifying the Insertion of Corneo-Sclero-Conjunctival Sutures in Operations for Cataracts, Tr. Am. Acad. Ophth. **38**: 434, 1933.

16. McLean, J. M.: A New Corneoscleral Suture, Arch. Ophth. **23**:554 (March) 1940.

17. Recently I have been using buried catgut sutures to close the deep wound, combined with silk sutures for closure of the incision in the conjunctiva. (Davis, F. A.: Catgut Sutures for Closure of the Deep Corneoscleral Wound in Operations for Cataract: A Preliminary Report, Arch. Ophth. **31**:321 [April] 1944.)

fourteenth day, since some patients do not return to the clinic for final refraction.

As shown in table 10, in 413 (82.6 per cent) of the cases visual acuity of 20/30 or better was obtained, while in 82 (16.4 per cent) visual acuity was classified as 20/40 or less. Careful study of the records of the 82 cases in which final vision was less than 20/30 reveals that in 51 the poor acuity was apparently due to preexisting intraocular disease.

Table 11 briefly summarizes the data in the cases in which visual acuity was less than 20/30, with the diagnosis to which the lowered acuity

TABLE 11.—*Analysis of Cases in Which Visual Acuity Was Less than 20/30* *

		Total No. of Cases
Poor vision entirely or partly due to preoperative disease		51
Diabetic retinitis (2 with slight loss of vitreous)....	14	
Chronic simple glaucoma (1 with loss of vitreous).	6	
High myopia	5	
Myopia with degeneration of vitreous (detachment 1½ years after operation)........................	1	
Senile macular degeneration........................	3	
Albinism with nystagmus........................	2	
Old corneal scars (interstitial in 1)........................	4	
Hypermature lens (15 years)........................	2	
Amblyopia (squint)	3	
Old retinal detach[illegible] (8 years)........................	1	
[illegible]	2	
[illegible]	1	
Complicated cataract (old iritis with synechiae)...	2	
Hypertensive retinitis, hemorrhage........................	2	
Juvenile cataract	1	
Polycythemia vera	1	
Subluxated lens (vitreous in anterior chamber, with slight loss)	1	
Poor vision attributed to postoperative complications....		15
Hemorrhage into anterior chamber........................	4	
Hemorrhage into anterior chamber; loss of vitreous (fluid)	1	
Hemorrhage into anterior chamber and vitreous...	2	
Keratoiritis	1	
Iritis, low grade; loss of vitreous, 4 drops..........	1	
Prolapse of iris........................	1	
Caught pillar	1	
Secondary glaucoma; bullous keratitis..............	1	
Corneal dystrophy	1	
Panophthalmitis (postoperative infection)..........	1	
Retinal detachment, 14 months after operation (original vision 20/15; small loss of vitreous)..	1	
No cause of poor vision found; no complications..........		7
Patient did not return for refraction; visual acuity taken on fourteenth day........................		9
		82

* The 82 cases represent 16.4 per cent of the 500 cases in which intracapsular cataract extraction was performed.

was attributed. As will be noted, diabetic retinitis, chronic simple glaucoma and high myopia account for the lowered visual acuity in one-half the cases. In the remainder, poor acuity resulted from a variety of causes, as enumerated.

In 15 cases vision of 20/40 or less was attributed to operative complications, as shown in tables 11 (second part) and 12. In 7 of these cases postoperative hemorrhage into the anterior chamber or the vitreous was responsible for the lowered acuity. In 2 of the remaining 8 cases postoperative iritis was the cause, in 1 of which there was loss of vitreous. In 2 cases there were prolapse of the iris and an incarcerated pillar. In 1 case corneal dystrophy was present. In 1 case secondary glaucoma with bullous keratitis occurred. In 1 case retinal detachment developed fourteen months after operation.[18] Vision was 20/15 at the time of discharge and, according to the patient, remained excellent up to the time of the detachment. There had been a loss of about 3 drops of fluid vitreous at operation. A similar loss of fluid vitreous occurred in the fellow eye, but vision to date (five years after operation) has been 20/20 in this eye.

In the entire series, 1 eye was lost as a result of infection. The patient had pus cells in the smear, but, through carelessness, the resident house officer failed to report it to me. We have had only 1 other case of intraocular infection

TABLE 12.—*Record of Visual Acuity in 15 Cases in Which Poor Vision Was Attributed to Postoperative Complications*

Vision	No. of Cases	Complication
20/40	2	Hemorrhage in anterior chamber
	1	Prolapse of one pillar of iris
	1	Caught pillar
20/50	1	Hemorrhage in anterior chamber
20/70	1	Hemorrhage in anterior chamber
	1	Loss of vitreous (fluid) and hemorrhage in anterior chamber
20/100	1	Hemorrhage in anterior chamber
	1	Keratoiritis
	1	Corneal dystrophy
20/200	1	Iritis, low grade, late; loss of vitreous
Hand movements	1	Hemorrhage in anterior chamber and vitreous
No vision	1	Retinal detachment (loss of vitreous) 14 months after operation
	1	Secondary glaucoma; bullous keratitis
	1	Panophthalmitis (postoperative infection)
	15	

during this period; this was associated with an extracapsular extraction. The patient, inciden-

18. Since this paper was written and the tables were compiled, a second instance of retinal detachment has been observed in a case of this series. It occurred three and a half years after operation, while the patient was shoveling coal.

During the past two years, in an additional 400 intracapsular operations performed since this series of 500 operations was reviewed, 3 additional cases of detachment have been encountered. Two occurred in 1 patient, in the first eye one year and in the second eye three months after operation. No vitreous was lost in either eye, and postoperative healing was prompt, with visual acuity of 20/30, maintained up to the time the detachments occurred. In the third case a detachment was noted one month after operation. The patient had pernicious anemia and suffered a cerebral vascular accident four months after the operation for cataract, while waiting in the hospital in preparation for an operation for reattachment of the retina. The operation was uncomplicated by either bleeding or loss of vitreous, and healing was prompt. Thus, we have had to date 5 cases of detachment in a series of 900 intracapsular operations, occurring three and a half years, one and a half years, one year, three months and one month respectively after operation.

tally, had had a successful intracapsular operation on the fellow eye four weeks before. He had chronic otitis media in one ear, of long standing, which had been brought under partial control by prolonged treatment in the department of otology. It is interesting that he escaped infection in the intracapsular operation but lost the other eye, operated on by the extracapsular method.

In 8 cases no definite cause could be found for the lowered visual acuity. In all cases the operation was without complication, and healing and the postoperative record were normal. Some of the patients spoke no English or other language that could be understood. Some were illiterate, and 1 patient was a malingerer and wanted a pension. There were not more than 4 cases in which loss of vitreous appeared to be the sole cause of poor visual acuity. In only 3 cases did secondary glaucoma develop.

A few other features deserve comment: In 1 case, that of a patient aged 82, scarlet fever with otitis media developed on the sixth postoperative day, with no interruption or complication in the healing process, and 20/20 vision was obtained. In another case mild otitis media developed. In 1 case erysipelas occurred on the seventeenth day, with no ocular complication and with final vision of 20/15 (Smith extraction). In 10 cases (possibly more) the patients were disoriented, in 2 so much so that their condition might be classed as postoperative mania. The disturbances in all cases cleared up promptly when the patch was removed from the fellow eye and the patient was allowed out of bed. In 1 case the patient fell out of bed on the eleventh day, breaking his hip; but his eye healed without complication, and vision was 20/15. In several cases restoration of the anterior chamber was delayed, in 1 case as late as the ninth day. Rest in bed and the use of a 2 per cent solution of pilocarpine hydrochloride daily was the only treatment employed. and in all cases healing occurred without further complication. In 2 of these cases delay appeared to be due to detachment of the choroid.

Failure of the deep wound to heal by first intention, with slight bulging of the wound under the conjunctival flap, was observed in a few cases, but, so far as I have been able to determine, in no case did actual postoperative prolapse or extrusion of vitreous occur. This indicates that a complete conjunctival flap with multiple conjunctival sutures will prevent rupture of the wound. The bulging under the flap proved to be due to aqueous in all but 1 case and usually disappeared by the twelfth to the fourteenth day. External oozing of thin serosanguineous fluid occurred in 3 cases, although the anterior chamber was not lost. No serious results followed except in 1 case, in which there was recurrent bleeding into the anterior chamber. No doubt a corneoscleral suture would prevent this separation of the edges of the deep wound.

True, or severe, iritis was observed in only 15 cases. No doubt there was a much larger number with mild irritation of the iris. However, when the patient was sent home on the fourteenth day with the ocular condition quiet, the postoperative reaction was not regarded, with rare exceptions, as iritis. In only 2 cases of iritis was the visual loss serious. In 1 of these cases, in which final vision was 20/100, there was severe keratoiritis, lasting three months. The patient had had no loss of vitreous. Similar iritis had followed an extracapsular extraction in the fellow eye, which was operated on elsewhere before the patient's admission to this clinic. The second patient had moderate loss of vitreous, with "hammock pupil," due to postoperative prolapse of the iris. Vision was 20/30 at the time of discharge, but a low grade iritis later developed, with reduction of vision to 20/200.

TABLE 13.—*Postoperative Iritis* *

Case No.	Vision	Time in Hospital	Comment
1	20/15	4 wk.	
2	20/15	39 days	
3	20/20	17 days	Mild iritis
4	20/200†	14 days	Vision 20/30 on discharge; "hammock pupil"; loss of vitreous
5	20/15	16 days	Low grade iritis
6	20/100†	3 mo.	Keratoiritis, severe
7	20/20	19 days	Low grade iritis; patient syphilitic
8	20/15	16 days	Late iritis, 1 month after discharge
9	20/30	20 days	Two drops of vitreous lost
10	20/15	30 days	Subluxated lens; no loss of vitreous
11	20/30	20 days	Low grade iritis
12	20/20	10 days	Mild iritis
13	20/20	3 wk.	Moderately severe iritis
14	20/30	3 wk.	Moderately severe iritis
15	20/20	20 days	Moderately severe iritis

* If the ocular condition was quiet and the patient was discharged within fifteen days, the case was not considered as one of true iritis, although in many instances postoperative irritation (low grade iritis) was present.

† Serious impairment of vision occurred in only 2 cases (4 and 6).

I am convinced that postoperative inflammation and iritis are much less frequently encountered with the intracapsular than with the extracapsular operation. This absence of postoperative irritation and inflammation in the great majority of cases is one of the most striking features of the intracapsular operation. Our record for postoperative vomiting coincides with that previously reported. It occurred occasionally when no postoperative sedative was used. We still avoid the use of morphine before or after operation, since it almost invariably produces vomiting. Codeine, ½ grain (30 mg.), and acetylsalicylic acid, 10 grains (0.6 Gm.), are the only sedatives used after operation, and they are avoided when possible. Pentobarbital sodium,

1½ grains (0.1 Gm.), is given by mouth one-half hour before operation.

The results of slit lamp studies, which were made before and after operation, differed little from those previously recorded.

Rupture of the hyaloid membrane, mushroom-like protrusions or strands were seen occasionally; also, holes in the hyaloid membrane were encountered at times. In 1 case a mushroom-like protrusion, without actual rupture of the hyaloid membrane, observed immediately after operation, has persisted unchanged for five years, with visual acuity of 20/20. In an occasional case a previously intact hyaloid membrane was observed to be ruptured, with extrusion of vitreous into the anterior chamber. Usually this was accompanied by no further complication, but in 1 instance low grade pain developed after this had occurred and persisted for some time. The first examination with the slit lamp after operation not infrequently revealed partial degeneration of the anterior portion of the vitreous. This was noted particularly in very old people. I have been unable to determine whether this condition existed before operation, and probably contributed to the development of the cataract, or whether it resulted from trauma incident to the extraction. This condition practically never interfered with healing, though visual acuity appeared at times to be affected by it.

Opacities in the deeper portion of the vitreous were commonly observed. Occasionally they were so pronounced that they interfered seriously with vision. The vitreous appeared to be fluid or partially degenerated in many of these cases. I assume that this condition existed some time prior to operation, though this could not be proved in all cases because of advanced changes in the lens on first observation. It was common in persons with high myopia. Pigment dust was frequently seen on the hyaloid membrane, and at times on the cornea.

In 2 cases pneumonia developed; 1 of the patients died, and the other recovered, obtaining 20/20 vision.

Records for astigmatism conformed closely to the average values observed after extracapsular operations. In this last series, of 300 cases, the average amount of astigmatism was 2.12 D. The highest was 5.50 D. (1 case), and the lowest, none (5 cases). No astigmatism was present in 5 cases; 1 to 2 D. of astigmatism, in 112 cases; 2 to 3 D., in 89 cases; 3 to 4 D., in 20 cases; 4 to 5 D., in 12 cases, and 5 to 6 D., in 1 case. There was no case of expulsive subchoroidal hemorrhage, although I observed this complication once during this period after an extracapsular extraction and once in a series of 400 additional intracapsular operations performed since the present series was reviewed.

COMMENT

The comments which conclude my former paper, based on the 200 cases reported at that time, need not be repeated here. Further experience with the additional series of 300 operations here recorded, as well as an additional series of 400 operations not yet reviewed, has served to convince me of the soundness of the intracapsular method of extraction. Once the technic is acquired, the operation is easier than the older method of capsulotomy, all things considered, at least in my hands. Loss of vitreous is no more frequently encountered, and need be no more common, than in the extracapsular operation. Healing in the majority of cases is far more rapid and attended with less complications than I have observed after the method of capsulotomy. Complications, of course, are inevitable in this, or in any other, method of operation, particularly when every patient is subjected to operation regardless of the outlook, so long as there is any hope of restoration of vision.

The technic of the operation as previously described has remained unchanged. My capsule forceps [19] were used in most of the operations, although the Arruga model is occasionally employed.

224 West Washington Avenue.

19. Davis, F. A.: Capsule Forceps for Intracapsular Cataract Extraction, Tr. Am. Ophth. Soc. **34**:239, 1936.

CHANGES IN THE FUNDUS OF THE EYE IN VARIOUS FORMS OF ARTERIAL HYPERTENSION

HERMAN ELWYN, M.D.
NEW YORK

The following changes in the fundus of the eye may be observed in many cases of hypertension: (1) edema of the retina and the optic disk; (2) cotton wool patches; (3) hemorrhages; (4) sharply defined white spots in the deeper layers of the retina; (5) glistening white spots and a star-shaped figure in the macular area, and (6) changes in the retinal vessels.

The pathologic basis of these changes may be described as follows: (1) for the edema, transudation of fluid from the capillaries into the substance of the retina; (2) for the cotton wool patches, accumulations of precipitated fibrin and serum; (3) for the hemorrhages, the presence of blood in the various layers of the retina, especially in the inner layers; (4) for the sharply defined white spots, deposits of hyalin, mixed with lipids and with lipid-containing fat granule cells in the deeper layers of the retina, and for some of the more superficial white spots, a ganglioform swelling of segments of nerve fibers in the nerve fiber layer; (5) for the glistening white spots. deposits of lipid and lipid-containing fat granule cells, and for the star-shaped figure in the macular area. deposits of hyalin and lipids along the fibers of the layer of Henle, which radiate from the macula.

These changes in the vessels are of two kinds: (1) functional, resulting in contraction of the arteries, especially of the secondary and smaller branches, and (2) organic.

The organic changes in the vessels are due to the following factors:

(*a*) Aging of the vessels. This process results in diminution of the elasticity of the vessel wall and, therefore, in lengthening of the vessel and widening of its lumen. In the retina this shows itself in irregular tortuosity of the vessel and in widening of the light reflex on the surface of the vessel.

(*b*) Arteriosclerosis. This process causes irregular thickening and nodular deformation of the arterial wall. It reveals itself in the retinal arteries as irregularities in the lumen and as an apparent compression of the vein where it is crossed by an artery. This apparent compression of the vein has been shown, especially by the histologic studies of von Sallmann, to be due, not to an actual compression of the vein, but to thickening of the adventitial coats of the artery and of the veins and to thickening of the common connective tissue layer wherever there is one. Irregular tortuosity of the vessels, widening of the light reflex, irregularities in the lumen and apparent arteriovenous compression are signs of aging and of arteriosclerosis.

In addition, there are occasionally arteries which have a silver white appearance in various portions of their course—the so-caller silver wire arteries. This appearance is due to a deposit of hyalin beneath the endothelium in the intima of the artery. This change is illustrated by Ballantyne, Michaelson and Heggie.[1]

The changes which have been enumerated occur in many cases of hypertension. All these changes together appear only in some cases; in others some of them are present, and, again, in other cases perhaps none at all. Before their association with the various forms of hypertension is discussed, it is necessary to find the common factor in the pathogenesis of these alterations: the edema, the cotton wool patches, the hemorrhages, the deposits of hyalin and lipids and the narrowing of the arteries. The changes due to aging and arteriosclerosis need no further comment.

COMMON FACTOR IN THE RETINAL CHANGES

One can obtain an insight into the pathogenesis of these retinal changes by recalling the results of the studies on the terminal vessel units by Ricker and his school. It was observed experimentally that when contraction of a small artery was produced dilation of the terminal vessels—the precapillary arterioles, the capillaries and the postcapillary venules—occurred after a certain time. As a result, the circulation in these terminal vessel units is slowed, and when the arterial contraction above is complete, stasis results. When the contraction is not complete, stasis does not result, but slowing of the circulation and

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1. Ballantyne, A. J.; Michaelson, I. C., and Heggie. J. F.: Tr. Ophth. Soc. U. Kingdom (pt. 1) 58:255, 1938.

diminution in the oxygen supply cause changes in the walls of the capillaries. At first the wall of the capillary becomes softened and permits fluid from the blood stream to pass into the tissues. Ricker spoke of this stage as peristasis. In a later phase temporary openings appear in the capillary wall and permit red blood corpuscles to pass through. This is the state of prestasis.

These principles in the general pathology of the blood vessels are exemplified in the retina in certain cases of hypertension, and the transudation of fluid and blood can be seen there as though produced experimentally. The narrowing of the arteries, the edema, the cotton wool patches and the hemorrhages indicate the occurrence of acute arterial contraction which is the result of dilation of the capillaries and the production of states of peristasis and prestasis. I shall speak of this condition as acute arteriospastic retinitis, or retinopathy. This, then, the arterial contraction, with the consequent dilation of the terminal vessel units, is the common factor in the pathogenesis of the visible retinal changes. When the arterial contraction is released, the arteries no longer appear narrowed, and the edema, the cotton wool patches and the hemorrhages gradually disappear. Such a process takes place, for example, in cases of acute diffuse glomerulonephritis with recovery.

When the arterial contraction persists for a sufficient time, the retinal tissue remains in a state of chronic deficiency of oxygen. Here, again, a fundamental principle of pathology finds expression in the visible changes in the retina. The deposits of hyalin and lipids and the star-shaped figure in the macular area are the result of the deficiency in the supply of oxygen, which, in turn, is due to the persistent contraction of the retinal arteries. I shall speak of this condition as chronic arteriospastic retinitis, or retinopathy. The ganglioform swellings of the nerve fibers in the nerve fiber layers have the same cause.

The acute and the persistent form of contraction occur in the retinal arteries in many cases of hypertension, in varying degrees. They account for the various combinations of narrowing of the arteries, edema, hemorrhages, cotton wool patches, deposits of hyalin and lipids and the star-shaped figure in the macular area. When the retinal vessels also show aging and arteriosclerosis, there are present, in addition, irregular tortuosity of the vessels, irregularities in the lumen and apparent arteriovenous compression.

VARIOUS FORMS OF HYPERTENSION

The various forms of hypertension may be classified as follows:

1. Essential hypertension in its benign phase.
2. Malignant renal sclerosis, or the malignant phase of essential hypertension.
3. Hypertension of renal origin.
   (*a*) Diffuse glomerulonephritis in its various forms (acute, subacute, subchronic and chronic).
   (*b*) In some cases of the more uncommon forms of renal disease, such as amyloid contracted kidney, unilateral renal hypoplasia, polycystic kidney, periarteritis nodosa with involvement of the vessels of the kidneys and hydronephrosis, pyelonephritis and prostatic obstruction.
4. Hypertension of preeclampsia and eclampsia of pregnancy.
5. Hypertension accompanying tumors of the adrenal glands and basophilic adenoma of the pituitary gland (Cushing's syndrome).

ESSENTIAL HYPERTENSION

Essential arterial hypertension is the form of hypertension that is most frequently encountered in the medical, as well as in the ophthalmic, clinics. In its clinical course the disease resembles chronic simple glaucoma. The latter condition begins to manifest itself in middle life, at the age of about 40, and occasionally earlier, with greater diurnal variations in the intraocular tension and with irregular periods in which the tension is increased. In time the greater diurnal pressures persist; the tension is high and does not return to normal without treatment, and eventually secondary changes occur in the eye. A similar course is seen in the cases of essential arterial hypertension. The normal arterial blood pressure is approximately 120 to 130 mm. of mercury, and 150 mm. is considered the upper limit of normal. In middle life, at the age of about 40, or slightly sooner, and occasionally at an early age, there occur greater diurnal variations of the blood pressure, and the pressure rises to 150 and 160 mm., only to return to normal at other times. With the passing of years the greater diurnal variations persist, but the blood pressure remains high, from 160 to 170 mm. In time it rises still higher, to 200 mm. and more, and finally persists at this level and cannot be reduced with treatment. Secondary arterial changes have now occurred.

Essential arterial hypertension also resembles chronic simple glaucoma in its essential nature. Glaucoma is a disease in which the physiologic mechanism for the maintenance of the intraocular tension, especially the central regulatory part of this mechanism, is inherently weak, and at middle

age, or earlier, it gradually loses its ability to maintain the normal intraocular tension.

Similarly, essential arterial hypertension is a disease in which the physiologic mechanism for maintenance of the normal blood pressure, especially the central regulatory part of this mechanism, is inherently weak as a result of hereditary influences and at middle age, or earlier, it gradually loses its ability to maintain the normal blood pressure. The hypertension is the central element of the disease. From the phase of the first greater diurnal variations in blood pressure to the period when the pressure remains permanently high, at 200 mm. or more, many years elapse—ten, fifteen or twenty years or more. It is for this reason that the disease is spoken of as benign hypertension. During the long early part of the period, in which the blood pressure gradually increases, no pathologic changes are present in the arteries anywhere in the body. The disease during this period is a definite functional one, an essential hypertension.

Such an increase in blood pressure can only be produced by the contraction of a large number of small arteries, and such a contraction occurs in the main effector organ for the maintenance of normal blood pressure, namely, the great vascular bed of the splanchnic region. Spastic contraction of the small arteries does not occur in any other organ in the body. This absence of spastic arterial contraction in such organs as the kidneys, brain, skin and eyes is of great importance, for it differentiates essential arterial hypertension, the benign form of hypertension, from other forms of high blood pressure.

It is obvious, therefore, that during the early years of essential hypertension there are no symptoms referable to any organ and no signs in the fundus of the eye which can be attributed to the hypertension. There is no spastic contraction of the retinal arteries, and therefore no signs of acute or chronic arteriospastic retinitis.

CHANGES IN THE LATER PERIOD OF BENIGN ESSENTIAL HYPERTENSION

In the later period of essential hypertension secondary changes, due to the persistent increase in blood pressure, manifest themselves in some arteries of the body. These changes occur practically always in the arteries of the kidneys and less frequently in those of the spleen, the pancreas and the brain. In the arteries of the kidneys there are observed (1) diffuse thickening of the intima of the smaller arteries, and (2) hyalinization with focal distribution of deposits of lipids in the smallest arteries, such as the terminations of the interlobular arteries and the afferent arteries of the glomeruli. This hyalinization and lipidosis of the prearterioles and arterioles in the kidneys give another name to the later phase of the benign form of essential hypertension, namely, renal arteriolosclerosis. These changes are much less frequent in the spleen and in the pancreas.

In the brain there occurs in the later stages of benign essential hypertension sclerosis of the larger vessels, especially those outside the brain proper. Within the brain, also, a subendothelial deposit of hyalin is focally distributed in segments of the small arteries. This hyalinization, which is also accompanied by deposits of lipids, corresponds to the arteriolosclerosis of the kidneys. When it occurs in the brain, the segment of the vessel is apt to form a miliary aneurysm, false or true, with eventual rupture and hemorrhages in the substance of the brain. This feature of essential hypertension has been studied especially by Spatz and his school. Such hyalinization occurs frequently, also, in the arteries of the choroid of the eye.

In the retina, as I have already mentioned, during the first period, of many years' duration, no changes referable to the hypertension are to be seen in the vessels, and of course none in the retinal substance. In the later stages, with the development of arteriolosclerosis in the kidneys and in the brain, there appear gradually in the vessels of the retina the changes due to aging and to arteriosclerosis, the production of which has been hastened by the chronic hypertension. There are then seen in the fundus angular tortuosity of the vessels, widening of the light reflex, irregularity of the lumen and apparent arteriovenous compression. Only rarely, and in the latest stage, does an occasional vessel show the white, "silver wire" appearance due to subendothelial hyalinosis.

The value to the physician of examination of the fundus of the eye in a case of the benign form of essential hypertension is primarily in the negative results. As long as there are only signs of aging and of arteriosclerosis in the vessels of the retina, and as long as there are no signs of acute and chronic arteriospastic retinitis, the disease is still in its benign form.

Complications.—However, complications may arise in the retina. The aging and the arteriosclerosis predispose the vessels of the retina to the following changes: (1) venous obstruction, more frequently of a branch, but occasionally also of the central vein; (2) obstruction of the central artery or of its branches, and (3) frequent or infrequent contractions of small arterial branches, with resulting small hemorrhages here and there in the fundus or with an occasional small area of edema or a cotton wool patch. The small vessels in the retina are especially liable to

occasional contractions in the course of essential hypertension in its later stages, and a few small, irregular hemorrhages, with an occasional cotton wool patch, are frequently seen in the retina in this stage. These are mild complications in the course of essential hypertension, but they point to a more important change.

I have said that acute and persistent spastic contraction of the retinal arteries does not occur in the benign form of essential hypertension. To this there are exceptions. In this disease, especially in the later stages, the arteries in many parts of the body are more labile and likely to undergo sudden contractions. This is particularly the case in the brain, where such sudden arterial contractions may give rise to temporary pareses and paralyses of the limbs, a possibility emphasized by Osler.[2] Frequently, such temporary pareses and paralyses are forerunners of permanent ones. In the retina, too, such arterial contractions are apt to occur in association with contractions of the cerebral vessels. When this happens, there appear in the retina the signs of acute and persistent spastic arterial contraction: namely, narrowing of arteries, edema, cotton wool patches, hemorrhages, deposits of hyalin and lipids and ganglioform swellings of nerve fibers. With the contraction of the cerebral arteries and the resulting edema in the brain there is increased intracranial pressure, with some swelling of the optic disks.

This change in the fundus is an added complication in the later stages of essential hypertension in some cases; when it is present, it places before the physician the problem of whether he is or is not dealing with the malignant form of essential hypertension. Continued observation alone can decide. When the occurrence of arteriospastic retinitis is only an episode in the late stage of benign essential hypertension, the spastic arterial contraction will recede under treatment. Also, the entire clinical picture must be taken into account. Episodal arteriospastic retinitis in the course of benign essential hypertension is not accompanied by any considerable renal insufficiency, and any renal insufficiency present will improve under treatment. Such episodes, however, foreshadow the eventual passing of the essential hypertension into a malignant stage, malignant renal sclerosis.

MALIGNANT RENAL SCLEROSIS, OR THE MALIGNANT PHASE OF ESSENTIAL HYPERTENSION

Essential hypertension in its ordinary, benign form lasts for decades, with relatively good health and normal renal function. Death is usually due to cardiac or cerebral disease or to an intercurrent disorder. In a number of cases, however, this phase passes into a malignant stage of hypertension. When this occurs, the clinical picture takes on the appearance of a new disease. This new hypertensive disease has been known by many names, such as malignant renal sclerosis, malignant hypertension, renal arteriolosclerosis with renal insufficiency and chronic hypertension with uremia. There is a fundamental difference between this form and the ordinary, benign form of essential hypertension. The malignant form is characterized by two important elements: (1) acceleration of the arteriosclerotic and arteriolosclerotic processes, especially in the kidneys, which led Klemperer to speak of this condition as the accelerated phase of essential hypertension, and (2) general arterial contraction, by which is meant that there is a persistent contraction of the small arteries, chiefly in the kidneys, but also in the spleen, pancreas, brain and eyes.

The acceleration of the arteriosclerotic and arteriolosclerotic processes is responsible for the occurrence of symptoms at an earlier age than with the ordinary, benign form. The acceleration may, according to Klemperer, possibly result from the arterial contraction, and is probably the cause of the severe changes in the large and small arteries in the kidneys, namely, the thickening of the intima, with its cellular and fibrous proliferation; the hyalin and lipid deposits, and the necrosis of the vessel wall, with nuclear disintegration and hemorrhages. The persistent arterial contraction in the kidneys is partly responsible for the renal insufficiency, and the contraction of the small arteries in the brain is responsible for the cerebral symptoms.

In the eyes, the persistent contraction of the small arteries is responsible for the changes in the retina. There are now apparent all the signs of arteriospastic retinitis: narrowed arteries, edema, cotton wool patches, hemorrhages, hyalin and lipid deposits and the star-shaped figure in the macular area. Edema of the optic disks is also present, due, first, to the contraction of the small arteries in the optic nerve and, also, to the increased intracranial pressure. Because the malignant stage of essential hypertension is preceded by a long period of high blood pressure, aging and sclerosis of the retinal vessels are also seen, with angular tortuosity of the vessels, irregularity of the lumen and apparent arteriovenous compression. The subendothelial hyalinosis is also observed in some of the arteries of the retina and gives the vessels their white, "silver wire" appearance.

2. Osler, W.: Canad. M. A. J. **1**:919, 1911.

These changes in the fundus of the eye, which are the result of aging, arteriosclerosis and acute and persistent contraction of the retinal arteries, are usually all present in cases of malignant renal sclerosis, or the malignant stage of essential hypertension. Variations in the fundic picture are due to variations in the individual factors. These changes when occurring in the presence of persistent renal insufficiency indicate a bad prognosis. Death is likely to occur within six months, occasionally later.

HYPERTENSION OF RENAL ORIGIN

In the hypertension which is the result of disease of the kidneys, the pathogenic factors differ from those of essential hypertension. In the latter, as I have previously stated, the hypertension is due to an inherited defectiveness of the mechanism for the maintenance of the normal blood pressure, especially of the central regulatory part of the mechanism. In hypertension of renal origin the central regulatory mechanism is also involved, but as a secondary and reflex effect from the kidneys. It will be recalled that a deproteinized plasma passes through the glomerular membrane by filtration, that for the purpose of filtration the kidney has an extremely sensitive pressure apparatus, that the force exerting the filtration pressure is the blood pressure and that when the blood pressure sinks to 40 mm. of mercury glomerular filtration ceases. The normal filtration pressure must therefore be maintained at all costs. It can be taken as a rule that whenever the normal glomerular filtration pressure is likely to be endangered, the organism responds at once with an increase in blood pressure. This is produced by a reflex from the kidneys over the central regulatory apparatus and by an arterial contraction effected by means of nerve impulses and hormones, such as renin or angiotonin. Such a danger to the normal intraglomerular filtration pressure occurs with diffuse glomerulonephritis in all its forms; in some cases of amyloid contracted kidney and polycystic kidney; in periarteritis nodosa when the renal vessels are affected, and in some cases of hydronephrosis, pyelonephritis and prostatic obstruction. Again, such a danger to the normal intraglomerular filtration pressure can be produced experimentally by narrowing of the lumens of the renal arteries, as has been shown by Goldblatt and his associates.

In all these forms of renal disease of which hypertension is a symptom there occurs contraction of the small arteries, which is usually general. It involves the small arteries of the kidneys, and probably those of other abdominal viscera and of the skin, brain and retina!

Glomerulonephritis.—In cases of acute diffuse glomerulonephritis the contraction of the small arteries in the skin is responsible for the pallor, and the sudden contraction of the small arteries in the brain is responsible for the headache, the convulsions and the occasional sudden loss of vision. In the retina the contraction of the arteries is shown by their narrowing, and with it are the signs of acute arteriospastic retinitis: edema, cotton wool patches and hemorrhages. The arterial contraction associated with acute diffuse nephritis is variable, with sudden steep rises and quick reductions in blood pressure. The pathologic features of acute arteriospastic retinitis are, therefore, also variable, the lesions varying from a few cotton wool patches and a few hemorrhages to the full blown picture. It may be recalled that acute diffuse glomerulonephritis is a disease of young people, and the signs of aging and of sclerosis of the retinal vessels are therefore not seen in such patients. The disease in its acute form does not last long, and in many cases recovery is complete. With recovery, the arterial contraction disappears; the blood pressure is reduced to normal, and all the signs of spastic retinitis disappear. When the disease is unusually prolonged, the signs of chronic arteriospastic retinitis, namely, deposits of hyalin and lipids and the star-shaped figure in the macular area, may be seen. These lesions, too, disappear with recovery. The changes in the fundus have practically no prognostic value with this condition. They signify only that the arterial contraction is also present in the retina and that it is either of short or of long duration.

With the subacute form of diffuse glomerulonephritis, which may last six months, and the subchronic form, which may last as long as two years, there appear in the fundus of the eye varying signs of acute and chronic arteriospastic retinitis. These signs differ with the degree and the duration of the arterial contraction and with the frequency of its recurrence in an acute form.

The chronic form of diffuse glomerulonephritis lasts from a few years to over twenty years. It is characterized by periods in which the disease is quiescent and the blood pressure either high or low, but stationary, and by periods of recurrent acute attacks. All possible combinations of the signs of acute and chronic arteriospastic retinitis may be seen in the course of the disease. With the passing of years the signs of aging and of sclerosis of the retinal vessels are added. In the advanced stage of the disease, with high blood pressure, renal insufficiency and the full blown picture of acute and chronic spastic retinitis, differentiation between this disease and

the malignant stage of essential hypertension may be difficult. The fundus picture alone is not sufficient to differentiate the two. In the case of either disease, when renal insufficiency is present the changes in the fundus indicate a poor prognosis, but the physician is aware of the poor outlook without knowing anything about the fundus.

It is of interest to remember that in many cases of chronic diffuse glomerulonephritis the disease may be present a long time, until termination, without hypertension. In such cases there is no arterial contraction in the brain or in the eyes. Examination of the fundus shows normal arteries and no signs of either acute or chronic arteriospastic retinitis.

Other Forms of Renal Disease.—Such conditions are not always accompanied by an increase in blood pressure. When hypertension is present, the symptoms, including the changes in the fundus, are those occurring in the course of chronic diffuse glomerulonephritis.

HYPERTENSION ASSOCIATED WITH PRE-ECLAMPSIA AND ECLAMPSIA OF PREGNANCY

In the clinical picture of preeclampsia of pregnancy hypertension is the chief symptom. This hypertension is not produced reflexly from the kidneys but is due to increased irritability of the regulatory center of the mechanism for the maintenance of normal blood pressure. The increased irritability of this regulatory center is an unwelcome secondary effect in some cases of pregnancy, and it lasts as long as there is increased irritability of the regulatory mechanism for uterine contractions. As a result, there is acute spastic contraction of the small arteries in many organs: the kidneys, other abdominal viscera, the skin, the brain and the eyes. The arterial contraction in the kidneys is responsible for the renal symptoms, and in the brain it produces the headache and the sudden amaurosis which occurs occasionally. The arteriospastic contraction is extremely variable and is liable to sudden changes. Sudden acute arterial contractions result in explosive symptoms, such as the convulsions which give eclampsia its name.

In the fundus of the eye the contraction of the arteries is shown by the narrowing of the vessels, which manifests considerable variability. The arterial branches are narrowed throughout their length, or segments of narrowing may alternate with segments of normal caliber. Dependent on the degree of arterial contraction, there are signs of acute arteriospastic retinitis: edema of the retina, cotton wool patches and hemorrhages. These, too, are variable, and only a few cotton wool patches and a few hemorrhages may be seen. Occasionally the retinal edema is of considerable extent, and the transuded fluid seeps through into the subretinal space and lifts up the retina. Preeclampsia is usually not permitted to exist for any length of time, and the symptoms of the more chronic arterial contraction, the hyalin and lipid deposits and the star-shaped figure in the macular area, are therefore not ordinarily observed. In rare cases they may be noted.

The changes in the fundus of the eye indicate the severity of the arterial contraction. As a guide to the advisability of artificial termination of the pregnancy the ocular changes are of less importance than the continuous observation of the state of the blood pressure.

The increased irritability of the regulatory center disappears with the cessation of the uterine contractions. With the complete involution of the uterus, all the signs in the fundus of the eye recede, with the other symptoms of preeclampsia and eclampsia.

HYPERTENSION WITH TUMORS OF THE ADRENAL AND THE PITUITARY GLANDS

Tumors of the Adrenal Gland.—Such tumors are rare. The clinical picture is characterized by paroxysmal attacks of blanching of the skin, palpitation, tachycardia, dyspnea and increase in blood pressure. The symptoms are due to an increased secretion of the hormones of the gland, which also produce arterial contraction in many organs, including the retina. The arteriospastic retinitis thus produced is said to resemble at times that of malignant renal sclerosis.

Basophilic Adenoma of the Pituitary Gland (Cushing's Syndrome).—This syndrome is characterized chiefly by adiposity, profuse growth of hair, plethoric appearance of the face, purplish red striae in the skin of the abdomen, the hips and the thighs, sexual dystrophy, polycythemia, osteoporosis of the skull and spine and arterial hypertension. The hypertension resembles that associated with adrenal tumors. It is possible that the increased production of hormones of the pituitary in cases of basophilic adenoma of this gland acts by increasing the production of hormones of the adrenal gland. In the 1 case of Cushing's syndrome which I had occasion to study there were no retinal changes. It is of course possible that with general arterial contraction an arteriospastic retinitis may be produced in this disease.

SUMMARY AND CONCLUSION

The changes in the retina which occur with the various forms of hypertension depend (1) on the contraction of the retinal arteries and (2)

on the degree and extent of their aging and arteriosclerosis.

Dependent on the persistence of the arterial contraction, the changes in the retina can be separated into acute arteriospastic retinitis, or retinopathy, characterized by edema, cotton wool patches and hemorrhages, and a more chronic arteriospastic retinitis, or retinopathy, characterized by deposits of hyalin and lipids and by the star-shaped figure in the macular area.

In uncomplicated essential hypertension in its benign form the retinal arteries are not contracted. The changes in the fundus of the eye are only those of aging and sclerosis of the retinal vessels. In the later stages occur complications, such as a few hemorrhages, occasionally a few white spots and occlusion of branches of the central vein and artery, occasionally of the main vessels as well. A more important complication is temporary arteriospastic retinitis, as part of a temporary arterial contraction in many organs. The clinical picture can be differentiated from that of the malignant stage of essential hypertension by the absence of any severe renal insufficiency.

In other forms of hypertension the fundus presents varying combinations of the signs of acute and chronic arteriospastic retinitis and of aging and sclerosis of the retinal vessels.

DISCUSSION

Dr. Herman Mosenthal, New York: Dr. Elwyn's paper has been one of the most comprehensive and appealing presentations that I have ever heard on the subject of morphologic changes in the eyegrounds associated with hypertension. I shall confine my discussion to the functional changes involved. One should recognize that there is no uniformity of opinion concerning the interpretation of the functional pathology of hypertension. Undoubtedly, there is spasm, or, more precisely, increased tonicity, of the arterioles and of the larger arteries when the blood pressure is elevated. A vexing question in this connection is whether the so-called spasm of the arterioles, resulting in "peripheral vasoconstriction," is the cause of or is secondary to the hypertension. The accepted idea is that it is the cause.

It is thought that the arterioles act as stopcocks to draw on the arterial pressure and regulate the supply of blood flowing to the capillaries. In all the organs that have been studied, that is, the kidney, brain, lung, skin and muscle, it is known that the arterioles do not maintain a constant diameter but that they distend and contract —even to the point of closure—in accordance with the physiologic needs of the tissue the blood supply of which they control. Also, the arterioles do not dilate and contract throughout the body as a whole but differ widely in this regard with each tissue. For instance, during a chill the blood vessels of the skin contract to a remarkable degree, while those in the deeper organs dilate. The same is true of exposure to cold. The blood supply also varies enormously with the activity of individual organs. This probably has been shown best by Richards, who observed that in the kidney as few as 5 per cent of the afferent glomerular arterioles may be open when the kidney is at rest and that 95, or even 100, per cent may be open when diuresis is produced. In view of all these observations, it seems illogical to assume that peripheral vasoconstriction involving the entire body is the cause of hypertension; rather, it is likely that the hypertension is produced elsewhere and that the peripheral vasoconstriction is secondary to the high blood pressure and serves the hypertensive person in the same way that it does the normal person, namely, to control the amount of blood flowing to the tissues so that normal function may proceed.

Medicine offers several good illustrations in support of the theory that constriction of the perpheral vessels is secondary to the degree of blood pressure which exists in the larger arteries. After the subtotal sympathectomy now in vogue for the cure of hypertension, it is found that the blood vessels of the retina dilate and assume a normal caliber, even though the sympathetic supply to the vessels of the eye is not severed. In other words, the lowering of the blood pressure due to the effect of sympathectomy on vessels in the body not involving the eye has brought about an adjusted physiologic dilation of the blood vessels of the retina, evidently in an effort to maintain a normal blood flow under the circumstances. It has been amply demonstrated that hypertensive retinopathy can be cured by subtotal sympathectomy and that the condition remains quiescent as long as the blood pressure is not elevated.

Another good example in support of the same interpretation, namely, that contraction of the arterioles is secondary, not primary, to the hypertension, is seen in cases of coarctation of the aorta, in which the pressure rises in the arms and in the head; this elevation of arterial pressure is, in all probability, due to narrowing of the aorta. (The enthusiasts who insist on ascribing all hypertension to renal ischemia point to the fact that the blood pressure also rises in the legs. The blood pressure in the legs, however, rises in a different fashion than it does in the arms. In the arms there is an increase in both the systolic and the diastolic pressure, while in the legs there is a rise in the diastolic, and not in the systolic, pressure. In other words, the pressure in the legs is the type characteristic of diminishing circulation, such as that associated with cardiac failure, the decreased blood supply to the legs being readily explained by the narrowed aorta.) The effect of the high arterial pressure on the peripheral vessels in the arms is constriction of the arterioles, so that capillary circulation is

maintained at a normal rate. In this instance the arterioles contract in response to hypertension, and are not the cause of it. This, again, illustrates how the musculature in the arterioles regulates the blood flow in the peripheral circulation and maintains it at a constant level regardless of the level of the arterial pressure.

Another illustration of the same mechanism is found in cases of extensive coronary thrombosis. In this condition the blood pressure drops for the undeniable reason that the heart is weaker than it was before the impairment. The decrease in blood pressure may be exceedingly great; yet in most cases the circulation in the periphery is maintained in normal fashion, evidence that the peripheral vessels dilate to accommodate themselves to the diminished arterial pressure and to allow a normal supply of blood to the capillaries. To put it in another way, contraction or dilation of the arterioles is a regulatory mechanism which accommodates itself to the rise or fall of the systemic arterial pressure.

That an increase in blood pressure causes the morphologic changes in the arterioles and in the larger blood vessels has been convincingly demonstrated by Goldblatt. He produced narrowing of both renal arteries and observed that the changes of necrotizing arteriosclerosis, which are the true signs of malignant hypertension, were present in all organs but the kidneys. The hypertension in this experiment made itself felt in all the blood vessels except those of the kidneys, where the blood pressure was not elevated because of the narrowing of the main renal arteries. Ordinarily, the kidney is one of the most vulnerable organs of the body in its reaction to hypertension, and the fact that it did not exhibit any changes in this experiment is conclusive evidence that the mechanical effect of the hypertension is responsible for the arterial and arteriolar changes which are common in cases of essential or renal hypertension in human beings.

239 Central Park West.

NERVOUS FACTOR IN THE ORIGIN OF SIMPLE GLAUCOMA

OTTO LOWENSTEIN, M.D., AND MARK J. SCHOENBERG, M.D.
NEW YORK

In another paper [1] we have stated that in cases of clinically unilateral simple glaucoma pupillary disturbances may generally be detected in the seemingly unaffected eye. These disturbances were found to be based on three factors: (1) modifications of the retinal receptors, (2) damage to the effector organs and (3) lesions in the central nervous system.

While in the early stage of the disease the first two factors were not constant, the third factor was always present. On the basis of new experiments, we shall discuss in this paper the origin and significance of the nervous factor. Is this factor sympathetic or parasympathetic, central or peripheral? Our studies were made both in cases of unilateral simple glaucoma, in which increase of tension has not yet occurred in the unaffected eye, and in cases of well developed glaucoma, both unilateral and bilateral.

RÉSUMÉ OF PREVIOUS STUDIES

Before analyzing the pupillary reactions to light characteristic of glaucoma, we shall recapitulate briefly some results of former pupillographic studies.[2] It is known that both the contraction to light and the redilation following it consist of various stages. The contraction begins after a latency period of 0.2 to 0.3 second; latency periods longer than this are considered pathologic. The period of contraction consists of three phases:[3] (1) a primary phase of about 0.4 second and an average speed of about 5 mm per second (fig. 1 *a* to *b*); (2) a secondary phase of about 0.3 to 0.4 second and an average speed of about 2 mm. per second (fig. 1 *b* to *c*), and (3) a tertiary phase, which is variable, of about 0.3 to 0.5 second and an average speed of 0.8 to 1.9 mm. per second (fig. 1 *c* to *d*).

The phase of redilation consists of a latency period, which is about equal to the latency period for contraction, a preliminary phase of dilation (fig. 1 *d* to *e*), and then a primary, (fig. 1 *e* to *f*), a secondary and a tertiary phase.

The light reflex of the pupil is usually considered parasympathetic. However, some features of the phases of contraction, particularly the secondary and the tertiary phase, are determined by the functional state of the sympathetic system, whereas the primary phase of contraction depends predominantly on the parasympathetic. Evidence for this is found in the fact that instillation of cocaine into the conjunctival sac improves the secondary and tertiary phases of the contraction period of the light reflex in cases in which these phases are poor. The primary phase of contraction of the light reflex directly expresses the influence of the third cranial nerve. A certain functional sympathetic tone is necessary to bring about not only a maximal sympathetic response, such as the psychodilation reflex, but a maximal parasympathetic response, such as the light reflex.

Poor sympathetic innervation facilitates the occurrence of symptoms of fatigue in the pupillary light reflex, and these sympathetically conditioned symptoms are characterized by gradual

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Pupillographic Studies: VII. From the Departments of Neurology and Ophthalmology, New York University College of Medicine.

This paper, in abbreviated form, was read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, on Jan. 17, 1944.

1. Lowenstein, O., and Schoenberg, M. J.: Pupillary Reactions of the Seemingly Unaffected Eye in Clinically Unilateral Simple Glaucoma: Pupillographic Contributions to the Diagnosis of Glaucoma in the Preclinical Stage, Arch. Ophth., this issue, p. 392.

2. (*a*) Lowenstein, O., and Friedman, E. D.: Pupillographic Studies: I. Present State of Pupillography; Its Method and Diagnostic Significance, Arch. Ophth. **27**:969 (May) 1942. (*b*) Lowenstein, O., and Levine, A.: Pupillographic Studies: V. Periodic Sympathetic Spasm and Relaxation and Role of Sympathetic Nervous System in Pupillary Innervation, ibid. **31**:74 (Jan.) 1944. For a better understanding of the principles applied in the present paper, the second article in particular should be referred to.

3. Gradle, H. S., and Ackerman, W.: Reaction Time of Normal Pupil: Second Communication, J. A. M. A. **99**:1334 (Oct. 15) 1933. The authors found a latent period of 0.1875 second. They detected a primary and a secondary (not a tertiary) phase of contraction, the former lasting 0.4365 second, with a rate of contraction of 5.48 mm. per second, and the latter lasting 0.3125 second, with a rate of 1.34 mm. per second.

fatigue diminution and early disappearance of the secondary and tertiary phases of contraction. However, another type of fatigue exists, due to damage to the nucleus of the third nerve; this is manifested, first, as an initial dilation preceding the contraction to light, and second, as an inhibition of the primary phase of contraction, which becomes sluggish. In cases of poor sympathetic innervation there develop hypersensitivity to cocaine and hyposensitivity to physostigmine, and in cases of hyperstimulation of the sympathetic fibers, hypersensitivity to physostigmine and hyposensitivity to cocaine. When the reflex to light is elicited by a weak stimulus, affecting only a relatively small number of retinal receptors, the first phase of contraction diminishes in extent (fig. 1 *B*, *a′ to b′*).

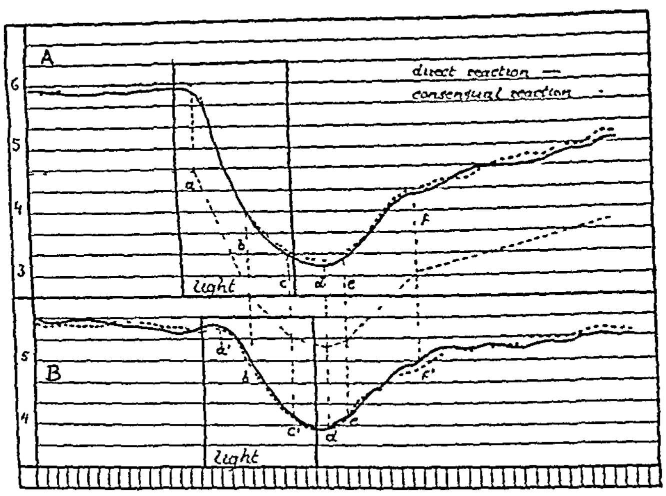


Fig. 1.—Influence of graded intensities of light stimuli on the different phases of contraction in a normal man, aged 53.

A, reflex to light elicited by a light stimulus of average intensity. A normal reflex is elicited, consisting of three phases of contraction (broken middle line): *a* to *b* indicates primary phase of contraction; *b* to *c*, secondary phase of contraction, and *c* to *d*, tertiary phase of contraction.

B, reflex to light elicited in the same subject by a light stimulus of low intensity (just visible).

All three phases of contraction are present: the primary phase, from *a′* to *b′*; the secondary phase, from *b′* to *c′*, and the tertiary phase, from *c′* to *d′*. While distance *b′* to *c′* is equal to distance *b* to *c*, and distance *c′* to *d′* to distance *c* to *d*, the primary phase (*a′* to *b′*) is only about one-fourth distance *a* to *b*. That is, differences in the intensity of the light stimulus produce differences in the primary phase of contraction but not in the following phases.

The latency period in *B* is slightly longer than that in *A*.

REPORT OF REPRESENTATIVE CASES

We distinguished four groups of cases; for every group a representative case is described.

First Group (fig. 2).—Case 1 (A. S.): This case is the same as case 2 of "Pupillographic Studies: VI."[1] In figure 2 are shown the reactions to light when the right, clinically normal, eye is stimulated, the left eye reacting consensually.

First Reaction: The first reaction, occurring after a latency period of less than 0.3 second, was nearly normal, although somewhat sluggish in all its phases. The primary contraction amounted to about 1.7 mm. in 0.4 second, the average speed being 4.2 mm. per second, instead of the normal rate of about 5 mm. per second. The secondary and tertiary phases of contraction together amounted to 0.6 mm. in 0.7 second, the average speed being 0.9 mm. per second, instead of the normal rate of 1.6 mm. per second. The spatial relation of the contraction of the pupil during the primary phase as compared with the contraction during the combined secondary and tertiary phases was about 3 : 1 (normal, 2 : 1). The ratio of the average speeds of contraction was about 4.6 : 1 (normal ratio, 3 : 1).

Second Reaction: But in the second reaction the ratio of the extent of the contraction in the primary phase to that in the secondary and tertiary phases increased to 8 : 1. The secondary and tertiary phases were practically absent, and this was still more noticeable in the third reaction to light.

In the third reaction to light the latency period increased to more than 0.3 second and was replaced by a slight initial dilation. At the same time, the speed of contraction in the primary phase was also decreased, but far less so than that in the secondary and tertiary phases. (In the second reaction the speed was 1.3 mm. in 0.4 second, or an average speed of 3.2 mm. per second, and it was still a little less in the third reaction.)

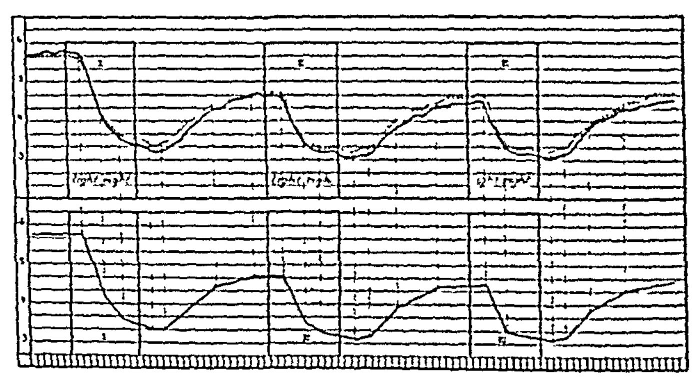


Fig. 2 (group 1).—Latent glaucoma in the supposedly unaffected right eye in a case of so-called unilateral simple glaucoma of the left eye.

First line: Three reactions of the right pupil to the light. The solid line indicates the direct reaction, and the broken line, the consensual reaction.

Second line: Scheme of the reactions, showing the phases of contraction and redilation.

First reaction to light: The three phases of contraction are present. The ratio of the amount of the primary phase of contraction, on the one hand, to that of the secondary and tertiary phases, on the other, is about 5 : 3.

Second reaction to light: The secondary and tertiary phases of contraction show a tendency to disappear but are still visible.

Third reaction to light: The primary phase of contraction is present to the same degree as that in the first and second reactions to light. A secondary and a tertiary phase are no longer distinguishable. The third reaction appears as though it were cut off at the end of the primary phase of contraction.

This case is characterized by the normal, although somewhat sluggist, first reaction of the pupil of the clinically unaffected eye to stimulation by light. The relation of the primary phase of contraction, on the one hand, to the secondary and tertiary phases, on the other, was also nearly normal. However, under the influence of repeated light stimuli, a disproportion quickly developed, so that in the second reaction to light the secondary and tertiary phases of contraction were practically absent, while the primary phase of contraction was comparatively only slightly fatigued.

Second Group (fig. 3).—CASE 2 (S. H.): This case is identical with case 1 in "Pupillographic Studies: VI." [1]—an instance of simple glaucoma in which clinically only the left eye was affected. We emphasized in that paper that pupillographic studies revealed that the right eye was also affected. In figure 3 are analyzed the pupillary reactions of both eyes, when the right eye was stimulated by light and the left pupil responded consensually.

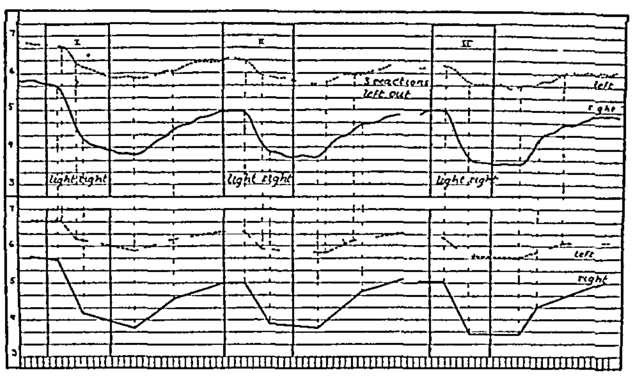


Fig. 3 (group 2).—Latent glaucoma in the supposedly unaffected right eye in a case of so-called unilateral simple glaucoma of the left eye.

First line: First, second and sixth reactions in a series of stimulations of the right pupil by light.

Second line: Scheme of the reactions, showing the phases of contraction and redilation.

First reaction: The secondary and tertiary phases of contraction are undistinguishable. The ratio of the contraction in the first phase to that in the following phases is about 4.5:1.

Second reaction: The secondary and tertiary phases of contraction are nearly absent.

Sixth reaction: The secondary and tertiary phases of contraction are entirely absent. The primary phase of contraction is practically unchanged.

First Reaction: It can be seen that the first phase of contraction was present, although somewhat sluggish. In the right pupil the contraction amounted to about 1.45 mm. in 0.35 second—an average speed of 4.1 mm. per second, instead of the normal rate of about 5 mm. per second. This phase was followed by a secondary and a tertiary phase, which together amounted to only 0.4 mm. in 0.9 second—an average speed of only 0.44 mm. per second, instead of a normal contraction of 1 mm. in about 0.6 second, or an average speed of 1.6 mm. per second.

The ratio of the change of diameter in the primary phase to that in the combined secondary and tertiary phases was about 4:1 (normal 2:1). The ratio of the average speeds in the phases under comparison was 9.3:1 (normal, 3:1).

Second Reaction: This ratio was further decreased in the second reaction to light, in which the secondary and tertiary phases of contraction were practically absent (0.1 mm. in 0.9 second), while the primary contraction amounted to 1.1 mm. in 0.3 second—an average speed of 3.6 mm. per second.

Other Reactions: The latency period for contraction, which was less than 0.3 second in the first reaction to light, had already increased to more than 0.3 second in the second reaction and had been replaced by an initial dilation in the fourth reaction. The fifth reaction, after a psychosensory stimulus which was interposed between the fourth and the fifth reaction, showed a slight degree of restitution, while the sixth reaction, again, showed complete absence of the secondary and tertiary phases of contraction.

In this case in the clinically normal eye there existed a disproportion between the primary phase of contraction, which was comparatively well developed, on the one hand, and the secondary and tertiary phases, which were poorly developed, on the other. This disproportion between the first and the subsequent phases of contraction increased under the influence of repeated stimulation with light. The speed of the primary phase of contraction was somewhat diminished. The latency period was increased in the first reaction to light, and an initial dilation preceded contraction as early as the fourth reaction to light. The secondary and tertiary phases were poor and had almost disappeared in the second reaction to light. While the disorders of the primary phase of contraction which occurred under the influence of repeated stimulation by light were relieved by psychosensory restitution, the disorders of the secondary and tertiary phases remained. The sixth reaction, for example, showed that, while the latency period was less than 0.3 second and the primary contraction amounted to 1.4 mm. in 0.4 second, with an average speed of 3.5 mm. per second, the secondary and tertiary phases of contraction were completely absent.

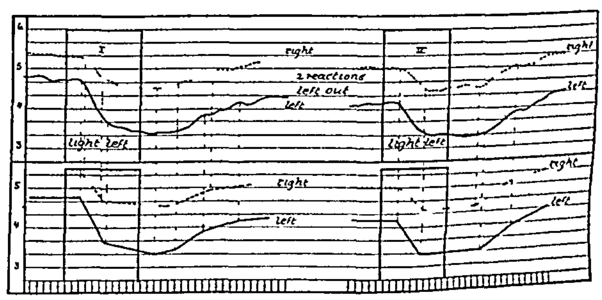


Fig. 4 (group 3).—Bilateral simple glaucoma, present to a higher degree in the right eye than in the left.

First line: First and fourth pupillary reactions of the left eye to light.

Second line: Scheme of the reactions, showing the phases of contraction and redilation.

First reaction: The secondary and tertiary phases of contraction are undistinguishable. The ratio of the first phase to the following phases is 3.5:1 in the direct reaction. For the consensual reaction of the right pupil the ratio is 2:⅓.

Fourth reaction: The secondary and tertiary phases of contraction are absent. The primary phase of contraction is somewhat diminished and more sluggish, as compared with the primary phase of the first reaction. Note the slight tendency to negative (reversed) secondary and tertiary phases of contraction, i. e., a slight dilation, instead of contraction, in the consensually reacting right pupil in the fourth reaction.

Third Group (fig. 4).—CASE 3: M. B. S., a woman aged 64, stated she had always been nervous, easily upset and easily depressed and that she had slept poorly ever since she was in college.

In October 1940 she had an attack of severe pain in the eyes, without blurring of vision or the seeing of rainbows. Two months later tonometric examination revealed a notable increase of intraocular pressure (35 mm., Schiøtz) in both eyes. Pilocarpine nitrate, in 0.5 per cent solution, reduced the pressure by 15 mm.

Neurologic examination showed overactivity of the deep reflexes, particularly the patellar responses and the reflexes of the upper extremities, but no organic factors were involved. Examination of the eyes revealed the characteristic signs of simple glaucoma. There were slight pallor and partial cupping of the right optic disk and slight pallor and shallow cupping of the entire left optic disk.

Perimetric examination showed paracentral defects. Repeated studies showed a tendency to enlargement of the scotoma.

Intraocular pressure was 30 mm. in the right eye. In the left eye it measured 28 mm. (Schiøtz) with a 7.5 Gm. weight, after use of a miotic had been discontinued for twenty-eight hours.

Vision was 20/15 + + in both eyes, correction with a + 2.50 D. sphere being prescribed for each eye.

On April 4, 1941, iridencleisis was performed on the right eye, and on May 12, on the left eye. Thereafter the intraocular pressure in the left eye remained normal (without the use of a miotic), while in the right eye it had a tendency to rise to 25 or 30 mm. This increase in pressure, however, responded to administration of prostigmine methylsulfate, 0.5-1 per cent.

There was slight anisocoria, the right pupil measuring 5.5 and the left pupil 4.85 mm. The contraction of the right pupil amounted to 0.6 mm. and remained at about the same level in the following five reactions.

The reaction of the left pupil to the first stimulus amounted to 1.3 mm., and in the following reactions the contraction was a little less than 1 mm.; the reaction to light after a sound stimulus was 1 mm. The latency period was more than 0.3 second in the first reaction and in all the subsequent reactions. The primary contraction of the left pupil to light, while the right pupil reacted consensually, amounted to 1.1 mm. in 0.4 second, with an average speed of 2.75 mm. per second; the secondary and tertiary contractions amounted to 0.25 mm. in 0.6 second, with an average speed of 0.4 mm. per second. The secondary and tertiary phases of contraction were almost absent in the second reaction and entirely absent in the fourth reaction. The ratio of change in pupillary diameter in the primary phase of contraction to that in the secondary and tertiary phases was 4.5: 1. The psychosensory restitution increased the amount of the primary phase of contraction, but not of the secondary and tertiary phases, and produced a sort of initial dilation.

The reaction of the right eye to light, while the left one responded consensually, did not show a secondary or a tertiary phase of contraction, even at the beginning. The latency period was more than 0.3 second. The primary phase of contraction, which was already sluggish, amounted to 0.6 mm. in 0.6 second, or an average speed of 1 mm. per second.

Fourth Group (fig. 5).—CASE 4: L., a physician, stated that since 1919 he had been suffering from glaucoma. He had had continuous headaches for many years but no fits. An operation (trephination) was performed in 1927 on both eyes, and a second operation, on the left eye, was done in 1935.

Neurologic examination showed that the deep reflexes were hyperactive, those on the left being slightly more active than those on the right.

The pupillographic picture showed that the diameter of the right pupil was 2.15 mm. and that of the left pupil 2.6 mm. The right pupil showed a latency period for contraction to light of more than 0.4 second. The primary phase of contraction of the right pupil was sluggish and inextensive, amounting to 0.3 mm. in 0.4 second (0.75 mm. per second), and that of the left pupil was 0.3 mm. in 0.6 second (0.5 mm. per second). The secondary and tertiary phases were completely abolished.

COMMENT

Analysis of the pupillary reflex to light in cases of simple glaucoma reveals certain constant characteristics. In cases in which clinically the disease is not yet well developed, or is not developed at all, as, for instance, in the supposedly unaffected eye in a case of unilateral glaucoma, the first symptom to be noted is a disproportion between the primary phase of contraction, on the one hand, and the secondary and tertiary phases, on the other. This disproportion is characterized by the preservation, to a greater or less extent, of the primary phase and the significant decrease, both in extent and in speed, of the secondary and tertiary phases.

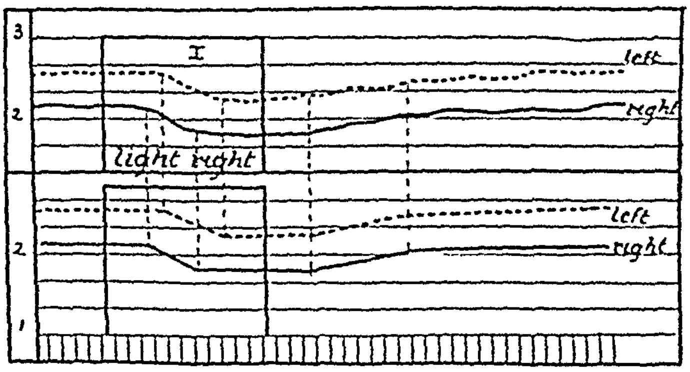


Fig. 5 (group 4).—Bilateral glaucoma, with small pupils and anisocoria.

First line: Reflex of the right pupil to light, the left pupil reacting consensually.

Second line: Scheme of the reaction, showing the phases of contraction and redilation.

The secondary and tertiary phases of contraction are absent. The primary contraction is greatly diminished, being inextensive and sluggish.

In certain cases of incipient or preclinical glaucoma the disproportion described is not yet present in the first reaction elicited by stimulation with light, but appears in the second, or even in the third, reaction, by which time a certain degree of fatigue has been attained (group 1). As the severity of the glaucoma increases, this disproportion, too, increases and is finally demonstrable in the first reaction to light (group 2). In the further development of the glaucomatous process, a third type of pupil-

lary reflex appears; in this response, the disproportion has further increased, and the primary phase of contraction has gradually become sluggish, while the latency period preceding contraction has increased, or has even been replaced by an initial dilation (group 3). In some cases, however, sluggishness of the primary phase and an increase in the latency period are present at a very early stage. But it may be stated that, in general, when the primary phase of contraction has become sluggish and the latency period is over 0.3 second, the secondary and tertiary phases of contraction have completely, or almost completely, disappeared (group 4). At that time the full characteristics of the light reflex of the glaucomatous pupil are present, i. e., a sluggish and inextensive pupillary movement, beginning after a long latency period (from 0.4 to 0.6 second), the primary phase of contraction being no longer followed by secondary and tertiary phases.

In another paper on glaucoma,[1] we discussed the reasons for our belief that damage both to the central nervous system and to the eyes produces the abnormalities present in the pupillary reflexes to light. We expressed the opinion that one is justified in the assumption that the lesions in the central nervous system are primary, although damage both to the effector organs and to the retinal receptors appears to be essential to an explanation of the pupillary picture in the final stages. However, we were unable to answer the question whether the peripheral lesions are secondary to the increase of intraocular tension or are simply associated with it; such an association would mean that all damage is the immediate and coordinate expression of the lesion in the central nervous system, perhaps through the mediation of the blood supply.

The high degree of sluggishness in the primary phase of contraction has been attributed to damage in the effector area, and the decrease in the extent of the primary contraction phase to retinal damage. Since we observed a number of cases of unilateral glaucoma in which no increase in intraocular tension had been observed in the unaffected eye, but in which nevertheless the pupillary light reflex showed typical glaucomatous modifications, the conclusion appears justified that intraocular tension is not responsible, or at least not solely, for the development of the glaucomatous type of reaction to light.

Another observation points to the same assumption.

A physician aged 49 had had a cyclodialysis performed on both eyes six years previously. Since the operation his right eye had remained hypotensive; the tension in the left eye had tended to rise to 35 mm. or more, but could be kept under control by the administration of pilocarpine. Pupillographic examination in this case revealed a characteristic disproportion between the primary phase of contraction and the following phases, which were almost absent, or at least greatly decreased. These characteristics were present in the responses both of the hypotensive and of the hypertensive eye (fig. 6). This observation gives evidence in support of the assumption that the characteristic disproportion in the phases of the light reflex cannot be due to the hypertension alone. In this case, however, the speed of the primary phase of contraction of the hypotensive eye seemed somewhat diminished (4.3 mm. per second). According to our observation, this may have been caused by damage of the muscle of the iris; this damage may have been due to the hypertension, which existed before the operation or, directly, to the same factor that caused the hypertension, or, lastly, it may have been the expression of modifications in the tonus of the sympathetic nervous system.

The explanation of our observations becomes possible in the light of the facts we mentioned earlier in the paper, and previously discussed in detail,[2b] namely, that the absence of the secondary and tertiary phases of contraction depends on disturbances in the sympathetic innervation and, furthermore, that a certain functional tonus of the sympathetic system is required to guarantee a maximal parasympathetic reaction.

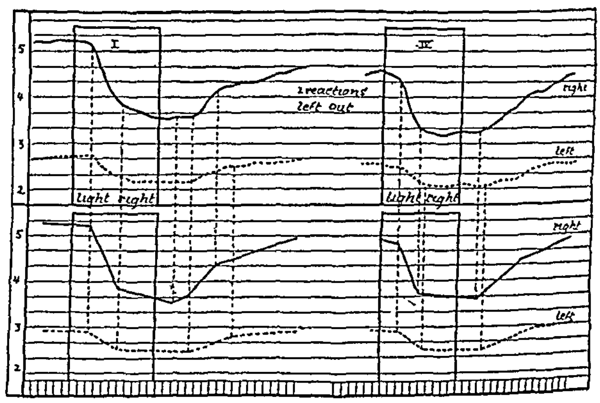


Fig. 6.—Bilateral simple glaucoma in a man aged 49. After previous cyclodialysis on both eyes, the right eye was hypotensive and the left eye hypertensive.

First line: First and fourth reactions of the right pupil to light, the left pupil reacting consensually.

Second line: Scheme of the reactions, showing the phases of contraction and redilation.

First reaction to light: The secondary and tertiary phases of contraction are undistinguishable. The ratio of the primary phase and the secondary and tertiary phases is 4 : 1.

Fourth reaction: The secondary and tertiary phases of contraction are absent, while the primary phase is practically unchanged (about 1.2 mm.). The consensually reacting left pupil shows only a primary phase of contraction, since the secondary and tertiary phases are completely absent. The primary phase of contraction is inextensive and sluggish.

On the other hand, the cases described here are, indeed, not characterized by simple absence

of sympathetic innervation, since the psychosensory dilation reflex was present, sometimes even in its full extent (fig. 7). In all these cases, however, another phenomenon, which generally is considered predominantly of central sympathetic origin, was either poorly developed or absent, namely, the psychosensory restitution phenomenon (fig. 7). This dissociation between psychosensory dilation (which remained) and the psychosensory restitution phenomenon (which was absent) suggests the conclusion that the damage should be sought not in the peripheral sympathetic pathways but in or above the central inhibitory sympathetic pathways passing to the parasympathetic nuclei. This assumption is in accordance with the fact that glaucoma could never be produced experimentally by simple section of the peripheral sympathetic pathways. Since the number of cases in which pupillographic examination has been made is relatively small, one can only state that glaucoma creates

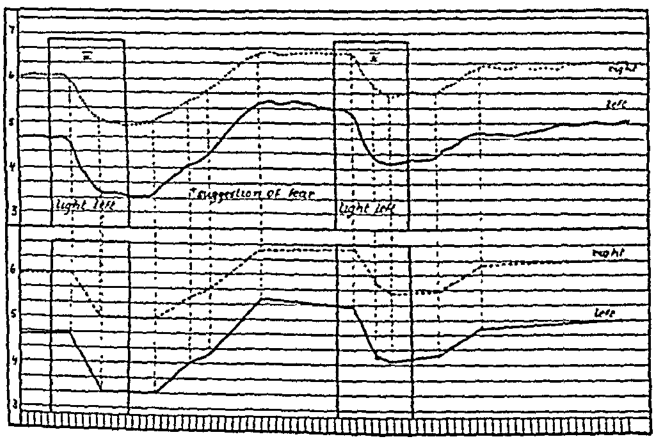


Fig. 7.—Unilateral simple glaucoma of the left eye. First line: Fourth and fifth reactions to light of the left pupil. Between the fourth and the fifth light stimulus a psychologic stimulus was interposed, which produced a good psychosensory dilation. The psychosensory restitution phenomenon, however, was poor.

Second line: Scheme of the reactions, showing the phases of contraction and dilation.

Fourth reaction: Absence of the secondary and tertiary phases of contraction.

Fifth reaction: Traces of a secondary phase of contraction reappear; however, the reaction soon changes to dilation. The primary phase of contraction remains sluggish and is not intensified, as compared with the first reaction.

pupillary disturbances which are primarily of central nervous origin; they are based particularly on lesions of those centers which take part in the sympathetic innervation of the pupil. At a very early stage, in which symptoms of glaucoma are not yet present or are slight, the pupillary reaction to light shows increased fatigability; this fatigability shows, as far as the phases of contraction are concerned, characteristics of the type one finds associated with weakening of sympathetic factors. At a more advanced stage the contraction to light is of the same type as that in cases in which the central sympathetic factors, normally effective in the phase of contraction, are completely absent.

This does not mean, of course, that pupillary disturbances are responsible for the development of primary simple glaucoma. But it does indicate that they are regularly associated with simple glaucoma. They frequently precede ocular hypertension and, as in the case of the supposedly unaffected eye of unilateral glaucoma, indicate lesions in the centers and pathways of pupillary control, as well as peripheral lesions in the receptor and effector organs. This means, possibly, that intraocular hypertension, pupillary disturbances, damage to effector organs, retinal lesions and the like constitute a syndrome in which all symptoms, intraocular hypertension included, are to be considered as equivalent expressions of the same lesion of the central nervous system. Within this syndrome, each symptom may be more or less developed, or even nonexistent, i. e., clinically not ascertainable.

According to the observations described here, it is certain that a central sympathetic factor plays a role in the genesis of primary simple glaucoma. It has not yet been shown, however, whether this central disturbance itself is primary, due, for instance, to a primary degenerative process in the central nervous system, or whether the degeneration itself is secondary to other etiologic factors, for example, nutritional deficiency or toxicosis. But it is certain that the lesion on which the syndrome depends lies within or above the inhibitory sympathetic pathways to the nucleus of the third nerve.

SUMMARY AND CONCLUSIONS

In all the cases of primary simple glaucoma studied, constant characteristics of the pupillary reflex to light were shown by both eyes.

In all the cases of the initial stage of the disease, the pathologic feature in the reflex to light was a disproportion between the primary phase of contraction, on the one hand, and the secondary and tertiary phases, on the other, the former being more or less preserved and the latter being decreased or absent. This disproportion is known to be due to a central sympathetic condition.

In all cases of advanced simple glaucoma, and frequently in cases of the initial stage as well, additional modifications were detected; the primary phase of contraction was sluggish and less extensive and was preceded by a longer latency period.

In cases of unilateral simple glaucoma the clinically unaffected eye showed pupillographic features characteristic of simple glaucoma. In some of the cases the pupillary disturbances were of purely central sympathetic origin; in others the sympathetic type was modified by ocular factors.

The occurrence of characteristic pupillary disturbances in the clinically unaffected eye points to the presence of latent glaucoma in that eye. This assumption involves the supposition that demonstrable increased intraocular pressure is preceded by centrally conditioned pupillary disturbances.

Intraocular hypertension is only one symptom *in a syndrome in which* ocular hypertension, lesions of the receptor and effector organs within the eye, and so on, exist as equivalent expressions of the same central lesion. Each symptom may be more or less developed, or even clinically unascertainable. This is true for intraocular hypertension (for instance, the latent glaucoma of the clinically unaffected eye in cases of supposedly unilateral glaucoma), as well as for other symptoms.

Although lesions of the central nervous system appear to be an important factor in the genesis of simple glaucoma, it is not certain whether such lesions, although organic, are primary or secondary to other etiologic factors, such as nutritional deficiency and toxicosis.

865 Park Avenue.
667 Madison Avenue.

DISCUSSION

Dr. Mark Schoenberg, New York: Two years ago I approached Professor Lowenstein with the problem of making pupillographic records in cases of simple glaucoma. So far, over 40 cases have been studied by this method, and the information derived therefrom has proved to be most interesting and useful. The results of this investigation may be summarized as follows:

1. I became convinced that pupillography detects disturbances of pupillary reflexes which cannot be discovered by the naked eye.

2. In all our cases there appeared anomalies in pupillary reactions which seemed to be characteristic.

3. Experiments on animals and careful analysis of pupillographic curves in cases of simple glaucoma revealed that the hypothalamus or its connections to the midbrain are mainly responsible for the anomalous reactions of the pupils. The pupillary factor is to be considered as a component of the glaucoma syndrome, just as are the other components, such as ocular hypertension and progressive optic nerve atrophy, all of them depending, directly or indirectly, on the central lesion.

4. In cases of so-called unilateral glaucoma in which clinically there were no signs or symptoms whatever in one eye, the pupillographic method revealed disturbances in both eyes.

Since the pupillary reactions in the good eye may be disturbed long before the appearance of other signs or symptoms, we are led to conclude that a preclinical stage is present in simple glaucoma and that its diagnosis may be established by the pupillographic method.

This method enables one to make a diagnosis in an early stage and in doubtful cases of glaucoma simplex.

Pupillographic studies must be continued in a large number of cases of glaucoma and of other diseases in order to clarify many questions connected with the problem.

Dr. E. D. Friedman, New York: All must pay a tribute of respect to Dr. Lowenstein for the industry and persistence with which he has followed this subject for the last twenty years, and for the great care with which he works. He and I have had a few chats on this subject, and I can perhaps offer him a bit of clinical confirmation of his thesis of the central origin of glaucoma. In 1923 I saw a patient, then aged 12 years, in Mount Sinai Hospital, and I followed her clinical course for twenty years, in the hope that some day I would have the opportunity to verify post mortem my clinical impression of the central origin of glaucoma. Unfortunately, however, the family did not cooperate. The patient had had bouts of fever and convulsions between the ages of 3 and 10 years, and at the time I saw her she also had external manifestations of dwarfism (stunted growth). Scleroderma-like changes were present in the skin of the lower extremities. The left eye was glaucomatous, with optic nerve atrophy, and five years later similar changes developed in the right eye. She presented oculomotor palsies first on the left side, and five years later on the right side. She also had periodic amenorrhea.

Later, there developed signs of involvement of the pyramidal tract (the Babinski sign and absence of the abdominal reflexes) on the left side, cerebellar symptoms and difficulty in upward gaze and in horizontal gaze to the left. All these signs and symptoms were interpreted as indicative of a lesion in the brain stem (the hypothalamic zone). The spinal fluid was normal. Roentgenographic examination revealed nothing significant except for bridging of the sella. The basal metabolic rate was — 15 per cent. Iridectomies had been done on both eyes, and she had only minimum residual vision.

I lost track of the patient for fifteen years, when I was informed that she had been admitted for oscillometric studies to the New York Post-

Graduate Hospital, service of Dr. Irving Wright. While she was there she had an episode of subarachnoid hemorrhage, from which she recovered. She returned home, where she died several months ago, evidently from another episode of subarachnoid hemorrhage. It was my belief in 1923 that possibly there was a disturbance in the central autonomic system, since the patient presented, along with signs of a lesion of the hypothalamus, involvement of the vasomotor system, scleroderma-like changes in the skin of the legs and glaucomatous changes in the eyes. I know that this is pure speculation, and I apologize for it, for I have no pathologic observations to corroborate my thesis; however, in view of Dr. Lowenstein's work and the fact that cerebral or psychic factors are known to exist in every case of glaucoma, I do not think it is being too bold to say that glaucoma may really have a genesis in the central nervous system.

PUPILLARY REACTIONS OF THE SEEMINGLY UNAFFECTED EYE IN CLINICALLY UNILATERAL SIMPLE GLAUCOMA

PUPILLOGRAPHIC CONTRIBUTIONS TO DIAGNOSIS OF GLAUCOMA IN THE PRECLINICAL STAGE

OTTO LOWENSTEIN, M.D., AND MARK J. SCHOENBERG, M.D.
NEW YORK

The cause of simple glaucoma remains unknown. It cannot even be stated whether the primary cause should be sought within the eye itself or outside the eye, as in the nervous system, or in both.

A series of observations point to the probability that disturbances of the central nervous system are to be considered among the pathogenic factors of glaucoma. Thus it seems justifiable to take a stand on the question whether the disturbances of pupillary reaction, which so far have been present in all cases (about 40) of glaucoma studied, are of central origin or whether they originate in secondary modifications of the receptor or effector organs in the eye.

In this paper we present the results of pupillographic studies in which one eye was clinically unaffected. The question arises: How do the pupillary reflexes of the seemingly normal eye behave, and what is the significance of their behavior?

REPORT OF CASES [1]

CASE 1.—S. H., a man aged 43 (fig. 1), had a family history of both parents having suffered from diabetes mellitus for about ten years. The patient had scarlet fever at the age of 22, without any known after-effects; influenza, with a high fever but without loss of consciousness, at the age of 24, and herpes zoster in the same year. He recovered from the last two illnesses, without after-effects, in about one week. There was no history of syphilitic infection. He had been married for twelve years and had 1 child, 7 years old. He had had hypothyroidism since 1938. He was easily tired and had to continue taking thyroid. Neurologic examination (Dec. 30, 1941) revealed no pathologic condition.

He was first seen by one of us (M. J. S.) on Oct. 24, 1940. The patient reported that the symptoms of glaucoma began in May 1940, after a period of cumulative excitement. He had frequent attacks in which vision was blurred in the left eye and he saw rainbow-colored halos around lights. Occasionally he had pains in the left temple. The use of pilocarpine cleared up the attacks of blurring and of seeing halos.

Ophthalmologic Examination.—Vision was 20/20 in the right eye and 20/25 in the left eye. Inspection of the fundi revealed a normal appearance of the right optic disk and slight pallor of the left disk, with engorged veins.

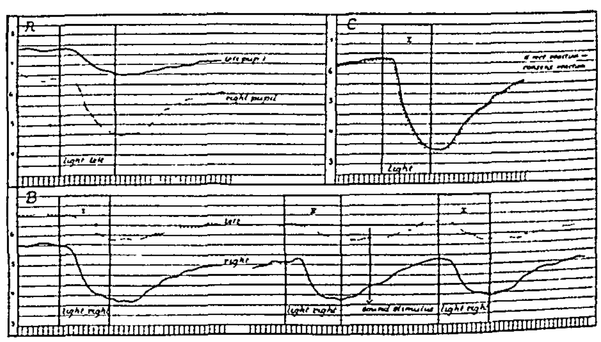


Fig. 1 (case 1).—Unilateral simple glaucoma of the left eye, in a man aged 43, the left pupil being larger than the right.

A, stimulation of the left pupil with light, the right pupil reacting indirectly.

B, stimulation of the right ("normal") pupil with light, the left pupil reacting indirectly. *I*, first reaction in a series of stimulations. The reaction is sluggish (as compared with that shown in *C*). *IV*, fourth reaction to light in the same series. The right pupil is excessively fatigable, with a latency period of about 0.4 second and a premature initial dilation preceding the contraction. *V*, fifth reaction to light in the same series. A sound stimulus is interposed between the fourth and the fifth reaction to light. The psychosensory restitution is poor. It is limited to restitution of the latency period, which appears shorter, while the initial dilation is no longer present. No deepening of the reaction itself occurs.

C, direct and consensual reactions to light of a normal subject (for comparison with *A* and *B*).

The intraocular pressure varied from 10 to 15 mm. of mercury in the right eye and from 10 to 15 mm. in the left eye as long as pilocarpine was used. After

This study was aided by grants from the Altman Foundation and the Oberlaender Trust.

Pupillographic Studies: VI. From the Departments of Neurology and Ophthalmology, New York University College of Medicine.

1. Recently one of us (M. J. S.) published a new classification of the stages of simple glaucoma. Four clinical stages were distinguished: (1) the functional, spontaneously reversible, stage; (2) the predominantly functional stage, with slight organic changes; (3) the predominantly organic stage, and (4) the completely organic stage. According to this classification, the disease in cases 1, 2 and 3 in this report was in the first stage, while the condition in cases 4, 5 and 6 was antecedent to the first stage, i. e., in the preclinical stage.

use of the miotic was discontinued for four days, the tension in the left eye was 28 mm. of mercury, and the eye became moderately congested.

Fields of Vision: There was slight disturbance at a tangent screen value of 1/1,000 mm.; repeated tests gave inconclusive evidence; the blindspots were enlarged.

Operation (April 1941).—An iridencleisis was performed on the left eye; recovery was uneventful.

Pupillographic Examination.—Inspection of the pupils revealed anisocoria, the diameter of the right pupil being 5.5 mm. and that of the left pupil 6.6 mm. The reaction of the left pupil to light was sluggish and less extensive than normal, with an extremely long latency period (more than 0.3 second). The contraction amounted to only 0.9 mm. The redilation, too, was sluggish. Psychosensory dilation and the psychosensory restitution of the left pupil were practically absent.

The pupillary response to light of the so-called normal (right) eye amounted to 1.9 mm. in the first reaction and to 1.2 mm. in the second and in the subsequent reactions. The right pupil was excessively fatigable. The latency period of the second reaction to light increased to about 0.4 second, and in the fourth reaction an initial dilation preceded the contraction (fatigue type). Both the psychosensory dilation and the psychosensory restitution phenomenon were poor. Both the contraction and the redilation showed pathologic features. While the reaction to darkness was almost absent on the left side, it appeared modified in its tertiary phase on the right side. The primary dilation was well developed.

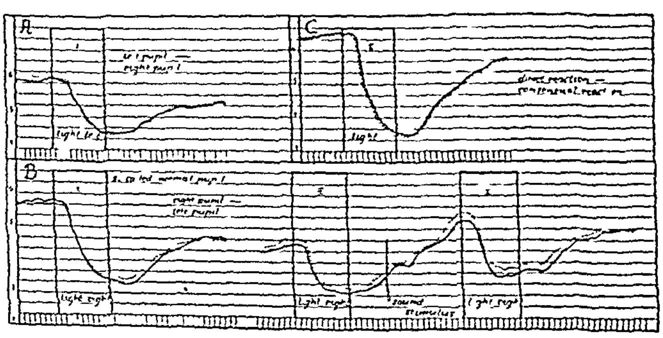


Fig. 2 (case 2).—Unilateral simple glaucoma of the left eye in a woman aged 59. The pupils were equal in size; however, slight anisocoria developed regularly after a certain number of stimulations with light.

A, reaction of the left pupil to light is slow; the latency period preceding contraction is increased, and the amount of contraction is only 1.6 mm.

B, pupillary reactions of the supposedly normal right eye. The contraction is slightly sluggish as compared with a normal one (*C*). Increased fatigability (fourth reaction) is characterized by a sluggish and small contraction after an increased latency period. Psychosensory dilation (after a sound stimulus interposed between the fourth and the fifth light stimulus) is well developed; psychosensory restitution, however, is poor. Note that the left pupil reacts better when stimulated indirectly than when stimulated directly. Slight dynamic anisocoria, however, is present after stimulation of the right pupil.

C, pupillary reflex to light in a normal subject (for comparison).

Case 2.—A. S., a woman aged 59 (fig. 2), had suffered from headaches for the past ten years but otherwise had never been sick. The menopause occurred at the age of 54. Neurologic examination showed no organic condition, but general nervous excitability was increased.

Ophthalmologic Examination.—Vision was 20/15 in the right eye and 20/20 in the left eye. Inspection of the fundi revealed pallor of the right optic disk and deep cupping and pallor of the left optic disk.

The anterior chamber of the right eye was normal, and that of the left eye was shallow.

Tonometric Examination: Pressure in the right eye was between 18 and 25 mm. of mercury without the use of a miotic. Pressure in the left eye was 35 mm. of mercury without a miotic and 18 to 25 mm. of mercury with a miotic.

Fields of Vision: The field of the right eye, as outlined on the tangent screen with a test object of 1 mm. at a distance of 1,000 mm. (1/1,000), remained good for

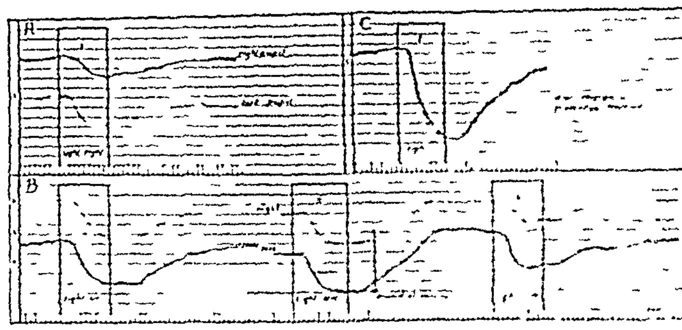


Fig. 3 (case 3).—Unilateral simple glaucoma of the right eye in a woman aged 46. The difference in the diameters of the pupils amounted to 1.6 mm.

A, reaction of the right pupil to light. Contraction, of no more than 0.6 mm., is preceded by a latency period of more than 0.4 second. The contraction is very sluggish. The consensual reaction of the left pupil is less sluggish and has a shorter latency period, but the contraction amounts to only 1 mm.

B, pupillary recation of the left, supposedly normal eye. The first contraction to light amounts to only about 1.6 mm. and decreases to less than 1.3 mm. in the following reactions. There is increased fatigability, and the latency period increases quickly to more than 0.3 second. Psychosensory dilation is well developed on both sides (after a sound stimulus interposed between the fourth and the fifth reaction to light), while psychosensory restitution is completely absent in both eyes.

C, pupillary reflex to light in a normal subject (for comparison).

two years. In the left eye the upper nasal field was defective. The patient had no complaints with respect to her right eye.

Both pupils were about 6 mm. in diameter. The left pupil reacted sluggishly to light, its contraction amounting to 1.6 mm. The latency period was increased. The redilation was slow. The psychosensory dilation and the psychosensory restitution phenomenon were present, although greatly diminished. The pupil of the right, or "normal," eye showed contraction to light of about 2.3 mm. While the type of contraction was fairly normal in the first reaction, it was quickly fatigable. The second reaction showed a latency period of more than 0.3 second, and the third reaction had an initial dilation. The psychosensory dilation was well developed. The psychosensory restitution phenomenon, however, was decreased. It is remarkable that the left pupil showed a contraction of 2.3 mm. in its indirect reaction but one of only 1.6 mm. in its direct reaction. The dilation to darkness was diminished on the left side and was normal on the right side. The secondary dilation, however,

was diminished on the right side also. In its indirect reaction, the right pupil reacted like the left pupil, and vice versa. The reaction to near vision was equal on the two sides.

CASE 3.—*C. G., a woman aged 46 (fig. 3), came under our observation on Sept. 11, 1942.*

She had been operated on for glaucoma in the right eye in December 1941. Twenty-four hours after the operation she had a sensation of paralysis of both upper and both lower extremities, lasting about five minutes. Since then, every morning on awakening, her eyelids seemed to be paralyzed for about forty seconds, so that it was temporarily impossible for her to open her eyes. Neurologic examination showed hyperactive patellar reflexes and diminution of vibration sense in the left leg. The neurologic diagnosis was "possible myasthenia pseudoparalytica gravis in its first phase."

Ophthalmologic Examination.—Vision was 20/20 in the right eye and 20/70 in the left eye. (The patient said her left eye had always been the poorer one.)

The anterior chambers were moderately shallow.

Inspection of the optic disks revealed optic nerve atrophy in the right eye, with deep excavation and engorged veins, and slight central cupping (physiologic) in the left eye, with pink color and slight engorgement of the veins.

Tension was 20 mm. of mercury (Schiøtz) in the right eye and 30 mm. of mercury (without use of a miotic for twenty-eight hours) in the left eye; with 2 per cent pilocarpine hydrochloride the pressure in the left eye became 25 mm. of mercury. This slight increase in tension without the use of a miotic was the only sign of glaucoma.

Fields of Vision: The upper half of the visual field of the right eye was contracted to 5 degrees from the fixation point. The left eye was normal.

Pupillographic Examination.—Inspection of the pupils revealed anisocoria, the diameter of the right pupil being 6.3 mm. and that of the left 4.7 mm. The right pupil showed contraction to light of 0.6 mm., after a latency period of more than 0.4 second. The redilation was slow. In its indirect reaction the right pupil contracted 1.2 mm., after a latency period of 0.3 second. Both the contraction and the redilation were less sluggish than those in the direct reaction.

In its first reaction the left pupil contracted to direct stimulation with light after a latency period of less than 0.3 second. The latency period, however, increased rapidly, while the contraction became sluggish. The contraction in the first reaction amounted to 1.6 mm. and that in the following reactions to less than 1.3 mm. The consensual reaction of the left pupil was more sluggish and less extensive than the direct reaction. The latency period for contraction was about 0.3 second in the first consensual reaction, and the extent of contraction was about 1 mm. Psychosensory dilation was well developed on both sides, particularly on the left. The psychosensory restitution phenomenon was practically absent bilaterally. The reaction to distant vision amounted to a dilation of 0.4 mm. on each side. While the reaction to darkness of the right pupil was diminished in its first phase of dilation on direct stimulation, it was present, although diminished, on indirect stimulation. On the other hand, the dilation to darkness was present in the left pupil on direct stimulation but was almost absent on indirect stimulation. The reaction to darkness of the left pupil was pathologic in its secondary dilation phase.

CASE 4.—*H. F., a man aged 52 (fig. 4), was first seen by one of us (M. J. S.) on April 21, 1924, when his eyes were observed to be normal. He returned on May 18, 1942, complaining that for the past month he "could not focus" his right eye and that he had occasional pains around that eye. He saw rainbows around lights and had noted a line or streak across them for the past five days.*

The diagnosis was noncongestive glaucoma of the right eye.

Ophthalmologic Examination.—The anterior chambers of the eyes were shallow, the depth being plus 3 in the right eye and plus 2 in the left eye.

The optic disks were of normal color; there was no cupping, and the veins were slightly engorged.

Vision was 20/15 in both eyes.

Visual Fields: The blindspot was moderately enlarged in the right eye and slightly enlarged in the left eye.

Tonometric Examination: The intraocular pressure measured 26 mm. of mercury in the right eye and 16 mm. with a 7.5 Gm. weight in the left eye. After one-half hour in the dark, tension was 30 mm. in the right eye and 15 mm. in the left eye. The tension of the right eye responded readily to administration of 2 per cent pilocarpine hydrochloride.

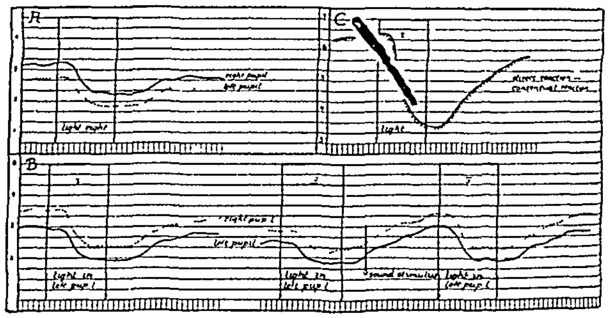


Fig. 4 (case 4).—Unilateral simple glaucoma of the right eye in a man aged 52. Anisocoria, with a difference of 0.5 mm. in the diameters of the pupils, was present.

A, reaction of the right pupil to light showing a long latency period (more than 0.3 second), followed by a sluggish contraction of only 1 mm. The indirect reaction of the left pupil is less sluggish.

B, reactions of the pupil of the left, supposedly normal, eye. An inextensive reaction of about 1 mm., following a latency period of more than 0.3 second, is rapidly exhausted. The fourth reaction is very sluggish, and the contraction amounts to 0.6 mm. The latency period for redilation after contraction is also prolonged. Psychosensory dilation (after a sound stimulus interposed between the fourth and the fifth reaction) is good on both sides. Psychosensory restitution (fifth reaction) is incomplete.

C, reaction to light in a normal subject (for comparison).

Neurologic Examination.—Slight differences appeared in the deep reflexes on the two sides, particularly in the patellar and triceps reflexes, which were exaggerated on the right side as compared with those on the left side. No symptoms of involvement of the pyramidal tract were noted, but muscle tone was increased on the left side. The Wassermann reaction was negative, and the personal history was noncontributory.

Pupillographic Examination.—Study of the pupils showed anisocoria, the diameter of the right pupil being 3.3 mm., and that of the left pupil 2.8 mm. The light reflex of the right pupil showed a long latency period

(more than 0.3 second). The contraction was sluggish and amounted to only 1 mm., and the redilation had a latency period of about 0.5 second. The indirect reaction of the right pupil was less sluggish, amounting to 1.15 mm. but having a latency period of 0.3 second.

The direct reaction of the pupil of the left, or so-called normal, eye was a little less sluggish than that of the right eye, but was rapidly exhausted, and its second reaction was deteriorated so as to show the same degree of sluggishness as did the first reaction of the right pupil. The latency period was more than 0.3 second. The indirect reaction of the pupil was more sluggish and less extensive than the direct reaction. The latency period for redilation after contraction to light was also prolonged to about 0.5 second.

Psychosensory dilation was good and psychosensory restitution was incomplete on each side. The reaction to near and to distant vision was equally disturbed on the two sides, as was the reaction to darkness.

CASE 5.—S. F., a man aged 50 (fig. 5), had had attacks of migraine since the age of 10 years; the pain was always on the left side, generally beginning in the late evening, before he went to sleep. In these attacks he was flushed and restless; the left side of his nose became congested, and he yawned frequently. After such an attack he was sick for a whole day. In 1930 he had the first attack of glaucoma, on the left side. There was no recurrence until ten years later, in 1940, when a similar attack occurred. The attacks had recurred every two to three months since.

Ophthalmologic Examination.—Vision was 20/20 in both eyes.

Examination of the fundi revealed no pallor or cupping of the optic disks.

The anterior chambers were shallow, the depth being plus 2 in both eyes.

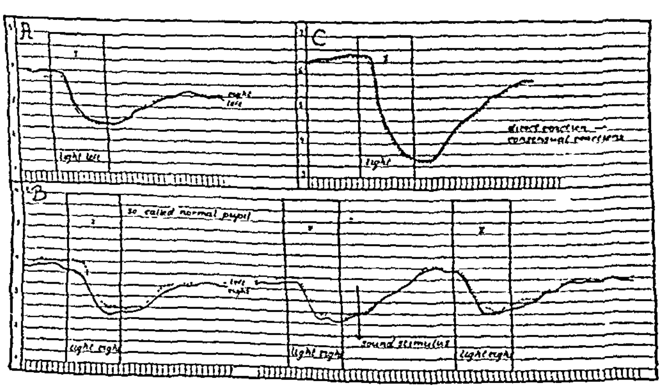


Fig. 5 (case 5).—Unilateral simple glaucoma of the ft eye in a man aged 50, with unstable anisocoria, e maximal difference between the pupils being 0.3 mm.

A, reaction to light of the pupil of the left, or glauomatous, eye. The contraction is sluggish and inexnsive, amounting to 1.3 mm. The direct and the onsensual reaction are identical.

B, pupillary reaction to light of the right, supposedly naffected, eye. The reaction is at least as sluggish s that of the left eye and is rapidly exhausted, the ourth response showing a latency period of more than .3 second. Note the dissociation between the directly eacting right pupil and the indirectly reacting left upil. Psychodilation (after a sound stimulus interosed between the fourth and fifth light stimuli) is good n both sides, and psychosensory restitution is poor (fifth reaction).

C, reaction to light in a normal subject (for comparison).

Tonometric Examination: The intraocular pressure varied from 20 to 17 mm. of mercury in the right eye and from 30 to 17 mm. in the left eye.

Visual Fields: Both blindspots were moderately enlarged.

Neurologic examination showed hyperactive deep reflexes, slight tremor of the fingers and a positive Romberg phenomenon, but no symptoms of true organic involvement of the nervous system.

The pupil of the left eye, 4 mm. in diameter, contracted after a latency period of 0.3 second. The contraction was sluggish and amounted to about 1.3 mm.

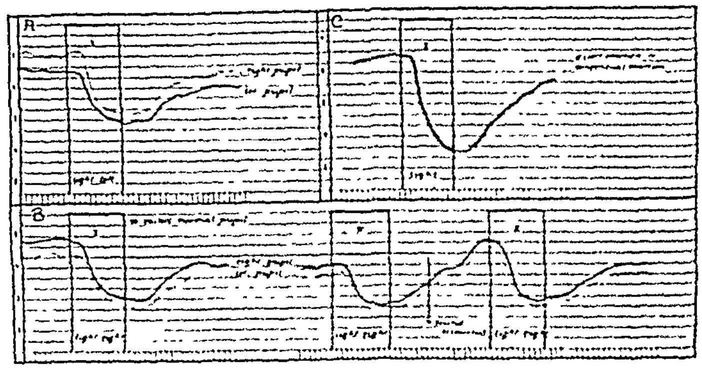


Fig. 6 (case 6).—Unilateral simple glaucoma of the left eye in a man aged 56. Anisocoria, with a difference in the pupils amounting to as much as 0.5 mm., exists.

A, pupillary reaction to light of the left, or glaucomatous, eye. The contraction is sluggish, amounting to not more than 1.6 mm., and is preceded by a latency period of more than 0.3 second.

B, reaction to light of the pupil of the right, supposedly unaffected, eye. The contraction in the first reaction to light amounts to about 2 mm. and fatigues rapidly, becoming more sluggish and decreasing to 1.3 mm. in the fourth reaction, while the latency period increases to more than 0.3 second. Psychosensory dilation (between the fourth and the fifth reaction to light) is well developed on both sides. The psychosensory restitution phenomenon, also, is comparatively well developed (fifth reaction); however, it disappears quickly. The pupillary contraction is followed by dilation while the light stimulus should still be effective—another symptom of poor restitution.

C, reaction to light in a normal subject (for comparison).

The reaction of the pupil of the right, so-called normal, eye was as sluggish as that of the left eye and was rapidly exhausted. Psychosensory dilation was good on both sides, and psychosensory restitution was poor. The reaction to near and to distant vision was good on both sides. The reaction to darkness was poor on both sides, particularly on the left side.

CASE 6.—S. D., a man aged 56, was first seen on Feb. 19, 1927, when he had no complaints or signs of glaucoma. Seven years later, in 1934, he first saw "rainbow-colored mists" around lights and had blurring of vision in the left eye. During the following years he had two to three attacks a year in the same eye.

Ophthalmologic Examination.—Vision was 20/30 in the right eye and 20/20 + in the left eye.

Examination of the fundi showed no cupping of the optic disks.

Tonometric Examination: The intraocular pressure was 20 mm. of mercury in the right eye and varied from 20 to 30 mm. of mercury in the left eye.

Visual Fields: The blindspot was moderately enlarged in both eyes, being somewhat larger in the right eye.

Pupillographic Studies.—There was slight anisocoria, the diameter of the left pupil being 4.7 mm. and that of the right pupil 5 mm. Contraction of the left pupil showed a long latency period of more than 0.3 second; it was sluggish and amounted to only 1.6 mm. The indirect reaction was better, the contraction being 1.7 mm.

The first direct contraction of the right pupil was approximately 2 mm., but the response rapidly became more sluggish and decreased to 1.3 mm. The psychosensory restitution phenomenon was comparatively well developed but disappeared quickly. Psychosensory dilation was well developed on both sides.

COMMENT

In these cases, and in others which we have studied but do not describe here, the pupillographic evidence indicates that pupillary disturbances limited to one side are not produced by simple glaucoma at all. Pupillary disturbances in simple glaucoma are always bilateral.

In most cases pupillary disturbances were more advanced in the glaucomatous eye than in the so-called normal eye. In no case, however, did the "normal" eye really show normal pupillary reactions. In several of our cases (3, 4 and 6) the pupillary reactions showed advanced disturbances on the so-called normal side, and in another (case 5) these disturbances were even more advanced than in the glaucomatous eye.

The question arises as to whether the pupillary disturbances allow one to draw any conclusions as to the location of the primary lesion which is responsible for them, either in the periphery (in the eye itself) or in the controlling organs of the nervous system.

Case 1 is particularly characteristic. The left pupil, i. e., the pupil of the affected eye, was larger than the right pupil. It contracted to light after a long latency period, and the reaction itself was sluggish and inextensive. The consensual reaction of the right pupil, however, was much less sluggish; its contraction was more extensive and more nearly normal, although it was still pathologic (fig. 1 *A*), as compared with a normal reaction (fig. 1 *C*).

The direct reaction of the right, supposedly normal, pupil (fig. 1 *B*) was also sluggish and inextensive as compared with a normal reaction (fig. 1 *C*). It fatigued quickly, as was readily shown by repeated stimulation with light; the fourth reaction showed all the symptoms of fatigue, i. e., a prolonged latency period, an initial dilation preceding contraction and a more sluggish contraction (fig. 1 *B*). The fatigued pupil, however, could be readily dilated by psychologic and sensory stimuli. The pathologically fatigued right pupil recovered (fig. 1 *B, V*) when a psychologic or sensory stimulus was interposed between the fourth and the fifth reaction. The fifth reaction was much better than the fourth, but did not yet show complete recovery, as is seen by comparison with the first reaction (fig. 1 *B*). These records demonstrate that the psychosensory restitution phenomenon was present in the supposedly normal eye, although to a decreased extent. The decrease in the psychosensory restitution was present, to a greater degree, in the diseased eye.

Can these modifications be explained by pathologic processes located within the eye? Such changes in the eye itself would be either in the light receptor organs of the retina or in the effector organs of the iris.

A. Damage to the Light Receptor Organs of the Retina.—When under the influence of a glaucomatous process, the cones of the retina are partly damaged; the original number of elements,

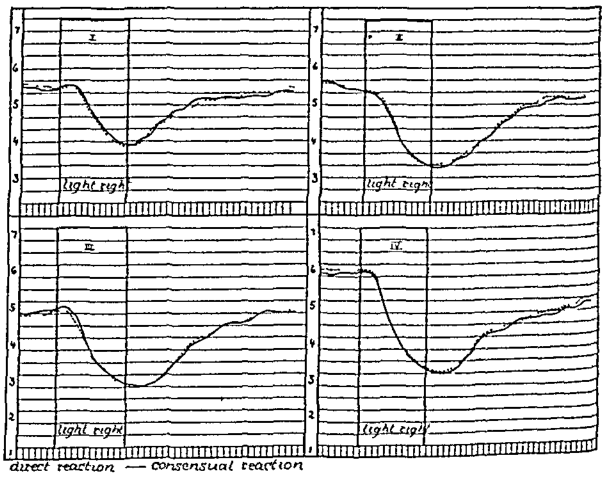


Fig. 7.—Varied pupillary reactions to light elicited by graded intensities of light stimuli in the same normal subject. The stimulus was always elicited by the same light source. The 100 watt, 6.5 volt bulb used was successively charged by 1 volt, 1.8 volts, 2.2 volts and 2.6 volts.

Reactions of different dimensions appear, the primary phase of contraction becoming longer the greater the intensity of the stimulus applied, while the secondary and tertiary phases remain identical.

The direct reactions are shown by solid lines; the indirect reactions, by dotted lines.

therefore, is no longer able to receive the stimulus and to conduct it. A pupillary reflex is still present but is diminished. One can duplicate such a condition fairly well by decreasing the intensity of the light stimulus which is directed, centrally or paracentrally, into the eye. According to the "all or none" law, the effect of stimulation is the same as long as the same number of elements are stimulated, regardless of the intensity of the light stimulus. It is to be expected, however, that the number of stimulated receptors

will decrease to the same degree to which the intensity of the stimulus is decreased; in this way, conditions become analogous to those in glaucoma in the event that the disease should have led to a partial destruction of the retinal receptors.

Figure 7 shows a series of experiments on the light reflex produced by each of a graded series of light stimuli in a normal subject. The applied light stimuli were always produced by the same light source, i. e., a 100 watt, 6.5 volt bulb successively charged by 1, 1.8, 2.2 and 2.6 volts.

It is evident that graded intensities of light stimuli elicit proportional variations in light reactions. It is also evident, however, that while the degree of contraction may be more or less decreased, the configuration of the light reflex remains the same regardless of the degree of light stimulation, that is, whether only a relatively small number of receptor elements are stimulated, or a greater number, or even all of them.

It is by these properties that the pupillary reaction of the normal eye is distinguished from that of the glaucomatous eye, which is not simply a normal reaction of diminished extent. This means that the modification of the configuration of the light reaction does not depend (at least, not exclusively) on possible modifications of the retinal receptors.

To this argument it could be objected that possibly an unequal distribution of the damaged elements exists in the glaucomatous eye, and that in the normal eye weak stimulation, when it was used, involved all elements of the fovea to the same degree. This objection, however, becomes invalid when weak stimuli are not directed into the eye centrally but come from a point in the periphery, so that chiefly the elements on the periphery of the retina are affected and the elements of the fovea are stimulated only weakly and irregularly, that is, to unequal degrees. In such experiments a modification of the reflex is not produced, but only a further diminution in the extent of the normal reflex of the pupil is effected.

B. Damage to the Iris.—It might be suggested that the pupillary changes associated with glaucoma are due to modifications in the iridal tissue. In that case, one must assume that the modification of the light reflex will be the same whether the eye is stimulated directly or indirectly.

Cases exist, it is true, in which both the glaucomatous eye and the supposedly healthy eye react equally poorly whether the stimulation is direct or indirect (figs. 1 and 6). In other cases of glaucoma, however, the same pupil differs in the degree to which it reacts, the extent depending on whether stimulation is direct or indirect (figs. 2 and 5). This means that the modifications of the pupillary reactions—both of the supposedly normal and of the glaucomatous eye—cannot be conditioned by damage to the iris. Therefore, one must assume the existence of two types of glaucoma, namely, one in which the iris is possibly involved and another in which the iris is certainly not involved.

In case 6 on stimulation of the glaucomatous eye with light, the consensual pupillary reaction of the supposedly healthy eye was better than the direct pupillary reaction of the diseased eye. This is evidence in support of the theory that in this case the receptors in the retina of the glaucomatous eye were not (or at least not solely) responsible for the pupillary disturbances. The direct pupillary reaction of the supposedly normal eye was poorer than the consensual pupillary reaction of the same eye—evidence that the condition of the iris certainly cannot be solely responsible, if at all. If the psychosensory dilation (the so-called ciliospinal dilation) is good in both pupils, it may be assumed that *the dilator fibers of the muscle of the iris* are not damaged. The psychosensory restitution phenomenon was incomplete on both sides with respect to the amount of the contraction, but was good with respect to the latency period and the speed of the contraction—evidence that the contraction fibers of the iris muscle cannot be seriously damaged, if at all.

Disturbances of the psychosensory restitution phenomenon are present on both sides in all cases, whether the pupillary damage is of lesser or of greater degree. This shows that if damage to the iris or the receptor elements is present at all, it must be, in any case, combined with central disturbances.

Case 4 was especially remarkable. The direct reaction of the right, or glaucomatous, eye was as extensive as the direct reaction of the supposedly normal eye. On the other hand, the pupil of the glaucomatous eye reacted better when stimulated indirectly, i. e., through the supposedly normal eye, than when stimulated directly. This might mislead one to the conclusion that disturbances of the receptors in the diseased eye were exclusively concerned. However, one is dealing not only with a diminished reaction, but with a pathologic modification of the reaction type, on both sides. Both pupils showed a good psychosensory dilation (ciliospinal reflex), an indication that at least the dilator fibers of the iris muscles were intact, and, since the pupils were very small (about 3 mm.) and contracted to less than 2 mm. it may also be assumed that the contraction fibers were intact. The psychosen-

sory restitution was poor (fig. 4 *B, V*), an indication that conditions of the central nervous system play a role.

All these facts and their evaluation suggest that, without recognizable rule, disturbances of retinal and iridal elements may occur in the supposedly *normal* eye which has *not* yet manifested glaucomatous disturbances clinically. They further suggest strongly that disturbances of the central nervous system play a role in all cases.

CONCLUSIONS

In all the cases of simple glaucoma studied pupillary disturbances accompanied the glaucomatous process, through *all* the stages examined, even the earliest. These pupillary disturbances proved to be bilateral; this was true even when clinically the glaucomatous process appeared to be unilateral.

Analysis of the pupillographic observations on the clinically unaffected eye in cases of unilateral glaucoma shows that a central nervous factor in the genesis of pupillary disturbances is always demonstrable.

While the central nervous factor is always present in the pupillary disturbances of the supposedly normal eye, functional modifications of either the retina or the optic nerve or both are frequently, but not always, present.

While we do not suppose that a causal connection exists between the pupillary disturbances and the glaucomatous process, we assume that both may be entirely or partially due to the same genetic factor, an assumption explaining the constancy with which pupillary disturbances accompany the glaucomatous process.

In view of (*a*) this constancy in the connection between pupillary disturbances and the glaucomatous process and (*b*) the fact that the clinically nonaffected eye in cases of unilateral glaucoma has so far shown pupillary disturbances, the pupillographic examination appears to promise a new way of establishing a diagnosis of glaucoma simplex in a preclinical stage.

865 Park Avenue.
667 Madison Avenue.

CAUSES OF IMPAIRED VISION IN RECENTLY INDUCTED SOLDIERS

CAPTAIN FREDERICK H. THEODORE, MAJOR ROBERT M. JOHNSON,
CAPTAIN NATHAN E. MILES AND CAPTAIN WILLIAM H. BONSER
MEDICAL CORPS, ARMY OF THE UNITED STATES

This report is the result of a survey undertaken to discover the causes of impaired vision in 10,532 of 190,012 recently inducted soldiers entering on basic training at Miami Beach, Fla. The survey was instituted at the suggestion and under the direction of Colonel Wilford F. Hall, Medical Corps, surgeon to the Station Hospital, Miami Beach Training Base. All the men were examined in the course of processing at the Eye Clinic of the station hospital. It should be understood that although the men came from all parts of the country, this study is not intended to represent a visual cross section of the eyes of American men between the ages of 18 and 36, as the induction boards had already eliminated enough of that group to make such a study impossible. Rather, the purpose of the investigation is to throw light on the pathologic reasons that the corrected vision of these men is below Army standards (20/40), usually in one eye, or sometimes in both eyes. In other words, if one excludes the men with correctible, purely refractive, errors, the report in the main is an ophthalmic classification of men placed in limited service because of their eyes.

The purpose of the visual processing was classification of the men for possible flying duty and for the various service schools maintained by the Army Air Forces Technical Training Command. When glasses were required, they were prescribed and ordered. In the processing, each man first had his visual acuity tested without glasses. Any glasses owned were then neutralized on the lensometer, and if vision with glasses was less than 20/40, the candidate was referred to the examining ophthalmologists and then subjected to refraction. In addition, men whose uncorrected vision was 20/40 or better, but not quite 20/20, received refraction in order that vision of 20/20 might be obtained for each eye and the inductee so qualify for certain types of flying duty.

Refraction for such large numbers of men made the routine employment of homatropine cycloplegia unfeasible, and its use was reserved for men with questionable vision, as well as for those who presented difficulties in examination of the fundus without mydriasis. A slit lamp was available, as were a perimeter and a tangent screen.

While the processing procedure was well planned and served its purpose of classifying large bodies of men with dispatch, and yet with considerable thoroughness, for the purposes of this survey several defects were noted in a review of the records. First, at times, especially during the early months of processing, no etiologic diagnosis was made. However, the only diagnoses significantly influenced by this policy were those of lesions of the macula (old central choroiditis) and corneal opacities. Sometimes, of course, an etiologic diagnosis was impossible. Perhaps the most important flaw in the survey was a tendency at the beginning, due to the unavoidable difficulties, to state merely in cases of amblyopia, that glasses did not improve a man's vision. As a result, a number of defects were classified as unexplained, rather than as refractive, amblyopia. The error thus introduced did not, however, alter any of the other categories and diminished as facilities were improved. One might estimate that under ideal circumstances probably not more than 5 per cent of the men recorded as having unexplained amblyopia would have been classified under refractive amblyopia. Organic diseases of the eye were ruled out in these subjects with amblyopia.

RESULTS OF STUDY

In 10,532 of the 190,012 men examined, it was found that vision in at least one eye could not be improved to 20/40. In table 1 are listed the main categories into which fell the ocular defects responsible for the visual impairment.

Amblyopia Due to Muscle Anomalies.—As noted in table 1, the amblyopia of a large number of men (24.22 per cent) was due to strabismus, either present or preexistent. This group represented 1.34 per cent of all the men examined. In addition to the usual classification, two types of lateral squint were differentiated: (1) squint with less than 10 degrees of arc, and (2) obvious squint.

Special care was taken in detection of small amounts of strabismus. If strabismus was not

From the Eye Clinic, Station Hospital, Miami Beach Training Base, Miami Beach, Fla.

present, but the patient gave a history of squint, which often had been corrected by operation, and no other cause for the amblyopia could be found, his case was listed under a special heading but was included with the amblyopias due to muscle anomalies. Of the men with hypertropia, several presented complicated defects, and their cases were listed under spasm of the inferior oblique muscle (paresis of the superior rectus muscle), as this frequent anomaly was also present in these cases. Although patients with alternating strabismus were not included in the survey, as they did not have amblyopia, the cases of 101 men were noted, 73 of whom had alternating esotropia and 28 alternating exotropia.

Table 1.—*Causes of Poor Vision in 10,532 Men*

	Total Number of Men	Percentage of All Men Processed	Percentage of Men with Poor Vision
Amblyopia due to muscle anomalies	2,551	1.34	24.22
Injury	1,907	1.00	18.11
Inflammatory disease	195	0.10	1.85
Degenerative disease	107	0.06	1.02
Congenital anomalies	246	0.13	2.34
Refractive amblyopia	2,620	1.38	24.87
Unexplained amblyopia	2,509	1.32	23.82
Cause of pathologic condition unknown	397	0.21	3.77
Total	10,532	5.54	

In table 2 are summarized the data on the men with amblyopia due to muscle anomalies.

Table 2.—*Causes of Amblyopia in 2,551 Men with Muscle Anomalies*

	Number of Men	Percentage of Series
Esotropia (noticeable)	1,002	39.29
Exotropia (noticeable)	349	13.68
Esotropia (slight)	657	25.75
Exotropia (slight)	160	6.27
Hypertropia (spasm of inferior oblique muscle)	89	3.49
History of previous strabismus	294	11.52

Trauma.—The important role that injuries play in the causation of visual defects is well known, but the large number of patients observed in this survey, 1,907, with impairment of such origin came as something of a surprise. In other words, 1 per cent of all the men who came through the processing unit had lost useful vision in one eye as a result of an injury. Trauma was the cause in 18.11 per cent of the 10,532 men with poor vision.

In order to simplify tabulation, especially when several pathologic conditions existed in an eye as the result of a perforating injury, the cases of all men with defects due to this cause were placed under the heading of perforating injury. In other words, a patient might present an adherent leukoma, incarceration of the iris, traumatic cataract and detachment of the retina all in one eye, as a result of the injury, but the case was classified simply as one of perforating injury. Moreover, enucleation and phthisis of the eyeball following such injuries were made subheads. Perforating wounds caused 44.08 per cent of all injuries. When the injury, usually a contusion, caused damage chiefly to one structure, it was classified as injury of that structure, such as traumatic cataract or central chorioretinitis following a blow. Subtypes of traumatic cataract were aphakia following operation or spontaneous absorption of the lens. The high number of macular lesions following trauma is notable and might even be augmented by some of the cases of macular lesions listed as of unknown origin.

Table 3.—*Types of Lesions in 1,907 Men with Histories of Injury*

	No. of Men	Percentage of Series
Perforating injuries of eyeball	842	44.15
Enucleation following perforating injuries	438	22.97
Phthisis of eyeball following perforating injuries	49	2.57
Other conditions following perforating injury	355	18.61
Atrophy of eyeball following contusion	9	0.48
Injuries to cornea		
Corneal opacities	141	7.40
Birth injuries (tears in Descemet's membrane)	11	0.58
Injuries to iris		
Occlusion of pupil	2	0.11
Injuries to lens		
Traumatic cataract	541	28.38
Aphakia following extraction of cataract	125	6.55
Cataracts not operated on	416	21.29
Subluxation of lens	14	0.74
Injuries to vitreous		
Opacities and organization following hemorrhage	4	0.21
Injuries to choroid and retina		
Detachment of retina	53	2.78
Hole in macula, following solar retinitis	3	0.16
Central chorioretinitis	213	11.17
Rupture of choroid	17	0.89
Diffuse choroiditis	3	0.16
Injuries to optic nerve		
Optic nerve atrophy	51	2.68
Avulsion of optic nerve	3	0.16

Inflammatory Conditions.—Old inflammatory conditions did not play an important role as a cause of poor central vision. Only 195 men, or 1.85 per cent of the men with poor vision, had had an inflammatory disease. Probably the cases of a large proportion of the men with corneal opacities and central choroiditis recorded as of unknown cause belong under this head; even so, their inclusion would not alter the percentage significantly. Inflammations of the uveal tract, of course, make up the largest group, as is shown in table 4. Needless to say, except in 1, or possibly in 2, cases of active choroiditis, the condition was quiescent.

Degenerations.—As was to be expected, degenerative diseases played a small part in this survey—107 men were affected, or 1.02 per cent, of

those with a pathologic condition of the eyes. If 64 men with myopic degeneration had not been included, the role of degenerative processes would have been even less important. Moreover, in some of the 15 men listed as having macular degenerations the condition was probably of inflammatory origin, although in some it was definitely degenerative and bilateral. On the other hand, it is not unlikely that additional men with early keratoconus, of which 11 were discovered, had sufficiently good vision that they were not referred to the ophthalmologist in the processing line. The same held true for pigmentary degeneration of the retina, which was noted in 12 men. Corneal dystrophy, 3 instances of which were recorded, may have been overlooked in a similar way. Miliary aneurysms of the retinal vessels, a rare condition, originally desecribed by Leber, was seen in 2 candidates.

Table 4.—*Types of Inflammatory Lesions in 195 Men with Poor Vision*

	No. of Men	Percentage of Series
Opacities following corneal inflammation		
Nonspecific opacities	37	18.97
Trachomatous pannus	2	1.03
Interstitial keratitis	1	0.51
Iritis	6	3.09
Uveitis	19	9.74
Choroiditis (except central)	20	10.25
Central chorioretinitis	41	21.02
Complicated cataract	15	7.69
Optic neuritis	2	1.03
Primary optic nerve atrophy	40	20.51
Secondary optic nerve atrophy	8	4.10
Recurrent hemorrhage in vitreous (Eales's disease)	2	1.03
Retinitis proliferans	2	1.03

Table 5.—*Degenerative Conditions Noted in 107 Men with Poor Vision*

		No. of Men	Percentage of Series
Keratoconus		11	10.26
Corneal dystrophy		3	2.79
Epithelial	2		
Endothelial	1		
Pigmentary degeneration of retina		12	11.20
Macular degeneration		15	14.00
Myopic degeneration		64	59.90
Miliary aneurysms of retina		2	1.85

Congenital Conditions.—As was to be expected, a wealth of congenital abnormalities were encountered in the processing. Two hundred and forty-six men with such defects, or 2.34 per cent of all candidates with poor vision, were seen. By far the most common anomaly was cataract, which was noted in 126 candidates. Next in frequency was atypical coloboma of the macula, also known as fetal central choroiditis, which was present in 38 men; under this head the cases of some of the men with unclassified forms of central chorioretinitis undoubtedly belonged. A large number of men, 32, had typical colobomas of all forms, involving the iris, the lens and the choroid, and sometimes the optic nerve. Six men had had corneal opacities since birth. In 4 of these, and possibly in a fifth, the lesion was undoubtedly of congenital origin and occurred with anterior synechiae. Other anomalies included bilateral aniridia, congenital retinal fold, medullated nerve fibers involving the macular region and hypertelorism. Additional anomalies are listed in table 6.

Table 6.—*Congenital Lesions in 246 Men with Poor Vision*

		No. of Men	Percentage of Series
Microphthalmos		8	3.25
Microcornea		2	0.81
Corneal opacities		6	2.43
Corectopia		1	0.41
Aniridia (bilateral)		1	0.41
Atypical coloboma of the macula (fetal central choroiditis)		38	15.45
Cataract		126	51.22
Subluxation of lens		2	0.81
Defects in closure of the fetal fissure		32	13.01
Coloboma of iris, choroid and lens	5		
Coloboma of iris and choroid	14		
Coloboma of choroid	2		
Coloboma of optic nerve	2		
Coloboma of optic nerve and iris	1		
Coloboma of iris and lens	1		
Coloboma of iris	1		
Coloboma of choroid and optic nerve	1		
Nystagmus		23	9.35
Medullated nerve fibers (extreme)		2	0.81
Persistent hyaloid artery		2	0.81
Partial aplasia of optic nerve		1	0.41
Pseudoglioma		1	0.41
Congenital fibrosis of lateral rectus muscle (Duane's syndrome)		1	0.41

Table 7.—*Refractive Amblyopia in 2,620 Men*

	No. of Men	Percentage of Series
Monocular refractive amblyopia	2,567	97.98
Binocular refractive amblyopia	53	2.02

Refractive Amblyopia.—Men with poor vision due to a high refractive error constituted the largest single group, numbering 2,620, or 24.87 per cent, of all those with a pathologic condition of the eyes. These candidates received generally more careful refraction than men with more easily correctible defects. Refractive amblyopia was present in one eye in 2,567 men and in both eyes in 53 men. As already mentioned, it is probalbe that some men with a condition recorded as amblyopia of unknown origin had refractive amblyopia.

Unexplained Amblyopia.—As was to be expected, men with amblyopia of unknown origin, with entirely normal ocular findings, formed an important group. A total of 2,509 men were encountered, or 23.82 per cent of all those with a

pathologic condition of the eyes. Of all the men processed, 1.32 per cent fell into this category. Monocular amblyopia was present in 2,495 men and binocular amblyopia in 14 men. In some of these men the condition was probably refractive amblyopia, but it is felt that few, if any, with organic disease of the eyes were placed in this group through error.

TABLE 8.—*Amblyopia of Unexplained Origin in 2,509 Men*

	No. of Men	Percentage of Series
Monocular amblyopia	2,495	99.44
Binocular amblyopia	14	0.56

Almost all of these men were checked carefully for possible malingering, and if any doubt existed as to the correctness of the results, the patient was returned for further study. Tests for malingering included the Wagner red, white and black chart, which requires only a red glass instead of the two color, red and green glasses usually used. As the patient's good eye is covered with the red glass and the supposedly poor eye is uncovered, there is less opportunity for him to cheat by closing it, unobserved. The mirror test, which doubles the distance of the letters from the patient, was of outstanding value, particularly in cases of binocular amblyopia. The value of routine confrontation tests should be particularly stressed; in both malingerers and persons with hysterical amblyopia these tests always revealed "tubular" fields, a pathognomonic sign. Relatively few malingerers or men with hysterical amblyopia were encountered in the processing. Instead, they were most frequently encountered on a return visit to the eye clinic for fancied ocular complaints, and detection was easier when there was a previous record of good vision. It is scientifically inaccurate, besides being unfair to the individual, to label a man as a malingerer, unless positive evidence is obtained: that is, the proving of normal vision by means of the special tests used. The tendency of examiners to classify a man as a malingerer merely because they can find no cause for the supposedly impaired vision is to be condemned except in rare instances.

Pathologic Conditions of Unknown Cause.—In this significant group are listed the men whose histories were too vague to permit an etiologic diagnosis and who presented a clinical picture which, likewise, did not indicate definitely the cause of the defect. This group included 397 men, or 3.77 per cent of all men with poor vision.

The most important condition encountered was old central chorioretinitis, which was noted in 263 men. In most instances the disease was probably inflammatory. In some men the condition was congenital, and probably in only a few was it of traumatic origin. Corneal opacities of unknown origin constituted another significant defect, being present in 128 men. Such lesions could probably be classified in the inflammatory or the traumatic category.

TABLE 9.—*Pathologic Lesions of Unknown Cause in 397 Men*

	No. of Men	Percentage of Series
Central (macular) chorioretinitis	263	66.25
Corneal opacity	128	32.25
Closure of central retinal artery	2	0.50
Old intraocular hemorrhage	2	0.50
Old retinal hemorrhage	1	0.25
Unclassified retinitis	1	0.25

Vascular accidents were also encountered, including closure of the central retinal artery in 2 men, old intraocular hemorrhage in 2 men and retinal hemorrhage in 1 man.

SUMMARY

Uncorrectible, impaired vision was encountered in 10,532 of 190,012 recently inducted soldiers.

Perhaps the most important result of the study was the observation that only one fourth of all men with poor vision had organic disease of the eye. In two thirds of the men with impaired vision of organic origin trauma was the etiologic factor, being usually the result of carelessness. In the case of the other three fourths it is possible that early care of the eyes might have prevented some of the resulting amblyopia, particularly the amblyopia resulting from strabismus and refractive amblyopia. When the condition was a pure amblyopia of unknown origin, it is less likely that early treatment would have been beneficial.

Thus, it seems fair to state that if proper attention had been given to the eyes of the 10,532 men studied, a significant percentage of the men might now be available for full, instead of limited, service. However, questioning revealed that with almost all the men with a neglected defect, especially those from large cities, where free care was readily available, the major factor was apathy, or even ignorance of the defect. Education, therefore, rather than the expansion of existing health facilities, appears to be needed.

CONJUNCTIVITIS AND KERATITIS OF ALLERGIC ORIGIN

ANALYSIS OF FIFTY-FOUR CASES

CAPTAIN WILLIAM O. LINHART

MEDICAL CORPS, ARMY OF THE UNITED STATES

According to O'Brien and Allen,[1] allergic dermatitis of the lids is not uncommon, but allergic keratoconjunctivitis is rare. Morrison[2] presented a verified case of allergic conjunctivitis and dermatitis resulting from the topical use of 5 per cent sodium sulfathiazole and 5 per cent sulfathiazole in a hydrous wool fat–petrolatum base. McAlpine and Berens[3] reported cases of blepharoconjunctivitis due to the use of tetracaine. Parlato[4] stated that allergy should be considered as an etiologic factor when chronic conjunctivitis, blepharitis and eczema of the lids have proved refractory to the usual treatment.

Balyeat and Bowen[5] classified allergic conjunctivitis as (*a*) the acute type, caused by animal dander, orris and eyelash cosmetics, and (*b*) the chronic type, divided in turn into the limbal and the palpebral form, caused by foods, pollens, animal dander, orris, dust and cosmetics.

Woods[6] discussed two steps in the diagnosis of responsible allergens—first, the taking of a history and, second, tests for the specific individual and group allergens. He expressed the belief that the best test is the intracutaneous injection of specific allergens.

The elimination of a certain element from local contact, from inhalation or from the diet with subsequent clearing of the lesion does not necessarily establish a diagnosis of allergy. In many cases in which allergic factors are suspected the observations on which a diagnosis is based are not conclusive. Patch tests, cutaneous tests for allergy and other necessary laboratory studies not only are difficult for the ophthalmologist to perform in the office but are somewhat out of his field.

In this series an attempt was made to select the patients in whose condition allergy was thought to be a definite factor. All but 5 of the patients were soldiers; all had primarily ophthalmologic complaints and were later referred to the allergist for a complete history with respect to allergy, a physical examination, cutaneous tests and an opinion.

History Analysis of Cases.—Twenty-three of the 54 patients, or 43 per cent, gave histories of allergy in the immediate family, while 10 in addition had close relatives with rather definite symptoms or diagnoses of allergic disease. Twenty had previous seasonal symptoms; these were worse in summer in 9 patients, in winter in 2 patients and in spring in 3 patients; the rest were troubled mostly in the fall. This observation may be compared with the results of Thomas and Warren,[7] who, in an analysis of 30 consecutive cases of allergic conjunctivitis, found that one third of their patients had a history of an allergic manifestation which had not been experienced in recent months. Eighteen of the present series of patients, or 33 per cent, gave indication in the history of previous allergic involvement of the eyes.

The recent change of environment which has accompanied the transfer of these soldiers from civilian to army life, in addition in many cases to a rather decided change of climate, may have had an influence on the present allergic condition.

Symptoms.—Lehrfeld[8] expressed the opinion that vernal conjunctivitis is a specific form of ocular allergy, and that if there is no itching, there is no vernal conjunctivitis. Twenty-five of the present series of patients had itching of the eyes or lids. Eighteen complained chiefly

From the Station Hospital, Fort Eustis, Va.

1. O'Brien, C. S., and Allen, J. H.: Allergic Keratoconjunctivitis, Arch. Ophth. **29**:600-604 (April) 1943.
2. Morrison, W. H.: Allergic Conjunctivitis and Dermatitis from the Topical Use of Sodium Sulfathiazole and Sulfathiazole, Am. J. Ophth. **25**:1104-1105 (Sept.) 1942.
3. McAlpine, P. T., and Berens, C.: Allergic Dermatitis (in Dentists) and Blepharoconjunctivitis Caused by Pontocaine, Am. J. Ophth. **25**:206-208 (Feb.) 1942.
4. Parlato, S. J.: Corneal Ulcers Due to a Common Allergen, Arch. Ophth. **14**:587-590 (Oct.) 1935.
5. Balyeat, R. M., and Bowen, R.: Allergic Conjunctivitis, South. M. J. **28**:1005-1011 (Nov.) 1935.
6. Woods, A. C.: Clinical Problem of Allergy in Relation to Conjunctivitis, Arch. Ophth. **17**:1-17 (Jan.) 1937.
7. Thomas, J. W., and Warren, W. A.: Analysis of Thirty Consecutive Cases of Allergic Conjunctivitis, Cleveland Clin. Quart. **7**:3-9 (Jan.) 1940.
8. Lehrfeld, L.: Vernal Conjunctivitis, Arch. Ophth. **8**:380-404 (Sept.) 1932; Eyelids and Conjunctiva as Shock Tissues in Allergy, Dis. Eye, Ear, Nose & Throat **1**:100-105 (April) 1941.

of watering of one or both eyes, and 18, of redness of the eyeballs. Fifteen said they had burning of the eyes, and 9 had as their chief complaint sore, itchy, swollen or irritated lids. Only 4 patients mentioned blurred vision.

Laboratory Data.—On examination, 35 of the patients were given Kahn tests of the blood, with negative results in all. One of the patients had previously had a positive Kahn reaction of the blood and at the time of examination was in the eighth month of antisyphilitic treatment.

TABLE 1.—*Types of and Reactions to Dust*

	Reaction			
	+	++	+++	++++
Dust, house	19	11	4	0
Dust, mattress	0	0	1	0
Dust, barracks	5	1	2	0
Dust, pine	1	5	0	0
Dust, warehouse and hospital	0	0	1	0
Dust, hospital	2	0	0	0

Teller,[9] in a study of 23 patients with vernal conjunctivitis, found that for more than 50 per cent the blood count revealed over 4 per cent eosinophils and almost all the patients had eosinophils in the conjunctival smear. Balyeat and Bowen [5] stated that smears usually show eosinophils.

Thirty-five patients in the present series had eosinophils in the blood, the average count being 2.9 per cent. The number of eosinophils varied from zero to 12 per cent. The patient with the 12 per cent count was referred to the gastroenterologist for clinical tests and examination of the stools in order to rule out the possibility that parasitic disease of the gastrointestinal tract was a causative factor. No evidence of parasitic disease could be obtained.

For 19 patients a differential count for eosinophils was made on smears of material from the conjunctiva, the average count being 4 per cent. The values varied from zero to 12 per cent. The absence of eosinophils in the smears of 11 patients brought the average to much lower than it would otherwise have been. For a patient with very acute keratoconjunctivitis the eosinophil count on the smear during the acute phase was 34 per cent. A similar count on a smear repeated at the end of one week, when the disease was in a more quiescent phase, revealed no eosinophils. The eosinophil count in general seemed to be much higher when the local reaction was more acute. No definite relation could be found between the eosinophil count of the blood and that of the smear, as the latter was likely to vary from day to day. Three of the patients for whom smears showed counts above 6 per cent had eosinophil counts of the blood averaging slightly over 4 per cent.

Five smears were taken from the conjunctiva, 3 of which showed no organisms and 2 gram-positive diplococci; 1 smear was negative for acid-fast bacilli. Of 14 cultures of material from the conjunctiva, 9 were sterile at the end of seventy-two hours; 3 showed Staphylococcus albus, with Staphylococcus albus haemolyticus in 1; 2 yielded Staphylococcus aureus, and 1, diphtheroid bacilli. It was thought that in these cultures the bacteria were either secondary invaders or contaminants.

Six patients had roentgenograms of the chest, and 7 had roentgenograms of the sinuses, with no significant evidence.

Data on Allergy.—Forty-nine patients had cutaneous tests against approximately ninety allergens, including bacteria. Of the patients not tested with the ninety allergens, 1 patient was tested with fifty-one allergens, 1 with thirty-three allergens and the rest with twenty allergens or less. The 3 women and several soldiers were given patch tests against suspected soaps or cosmetics.

As may be seen in tables 1 and 2, the results were classified as reactions to dust, the most common causative allergen, and reactions to the next ten most common allergens. It was felt that since dust itself and sensitivity to dusts are extremely prevalent, the reactions to such substances must be considered from a different standpoint than those to the other allergens. The sensitivity reactions to specific forms of dust are indicated in table 1. The results of tests for the common allergens are shown in table 2. In many cases in which sensitivity reactions of only 1 or 2 plus occurred, the ocular signs were the only physical indications of allergy. According

TABLE 2.—*Reactions to the Most Common Allergens*

	Reaction			
Allergen	+	++	+++	++++
Coffee	21	9	8	6
Feathers	13	16	3	1
Buckwheat	6	8	10	0
Tobacco	20	7	5	0
Banana	14	15	1	0
Barley	16	5	6	0
Wool	17	9	1	1
Cherry	30	4	1	0
Pyrethrum	15	9	2	0
Asparagus	12	6	5	0

9. Teller, I.: Allergic Investigations on Twenty-Three Cases of Vernal Conjunctivitis, Am. J. Ophth. **16**:149 (Feb.) 1933.

to Blank,[10] such a condition probably represents an ocular manifestation of allergy only, and the sensitivity would be demonstrated in other forms if the reaction were more pronounced.

Acute reactions (+ + + +) were obtained for the following allergens in 1 patient each: sycamore, horse serum, corn meal, tomato, monilin, buckwheat, feathers, wool and rabbit. Two patients showed 4 plus reactions to trichophytin. It is interesting to note that in only 2 patients who gave 4 plus reactions was the allergen one of the ten most common allergens.

Woods[6] stated that it is important to make local ophthalmic tests with a 1:10 or a 1:100 dilution of the strength used for cutaneous tests when there is doubt as to the specific allergen. Ophthalmic tests were made on only 1 patient in this series.

Physical examination for allergy revealed asthma in 7 patients and allergic rhinitis in 10 patients, as well as ocular signs of allergy, such as allergic dermatitis of the lids (4 patients), scars of old keratitis of possible allergic origin (2 patients) and chronic vernal conjunctivitis (3 patients).

Physical Signs.—The conjunctival and corneal signs varied with the acute, chronic and recurrent types of allergic involvement. In the acute form of allergic conjunctivitis, the conjunctiva was moderately injected and slightly edematous, particularly on the palpebral surfaces, the process being more conspicuous in the lower cul-de-sac. Balyeat and Bowen[5] observed uniform injection of the conjunctiva, occasionally localized, with the acute type. This localized area of congestion, which was seen in several of our patients, simulated somewhat a phlyctenule on the bulbar conjunctiva and was comparable to an urticarial wheal of the skin. In 1 patient an area of edema extended into the cornea approximately 3.5 mm., the superficial half of the cornea being involved. Small or large follicles might or might not be present in the lower cul-de-sac. Their presence was not a diagnostic aid.

With the recurrent and chronic types, follicles were common, and both the upper and the lower palpebral surface of the conjunctiva were usually granular. The commonest feature of the chronic type was a velvety, boggy appearance of the palpebral surface, which was more pronounced in the lower cul-de-sac. Stringy mucoid discharge was usually present, in contrast to the watery discharge seen with the more acute type.

The classic cobblestone appearance of the conjunctival surface of the upper lid was presented by each of the 3 patients with vernal conjunctivitis.

It was surprising to find corneal involvement on examination with the slit lamp in many of the patients who seemed to have only conjunctivitis on gross inspection and examination with the loupe. Seventeen of the patients had gross corneal lesions. The majority of the early corneal lesions could be detected only with the slit lamp after the cornea was stained with a 1 per cent solution of fluorescein sodium. Small superficial stained areas were more noticeable on the surface 1 to 1.5 mm. from the limbal margin of the cornea on gross inspection and near the normal extensions of the vessels on examination with the slit lamp. As the condition progressed, these areas coalesced; infiltration became deeper, and discrete gross ulcers formed. The superficial vessels of the conjunctiva bordering on the lesion first became engorged, and later extended on to the cornea toward the infiltrated area (figure). Usually the infiltration and the surrounding edema increased in all directions, extended to the limbus and had a tendency to form an incomplete ring bordering on the limbal margin.

In several patients numerous gross erosions, with underlying infiltrations, were scattered throughout the cornea. During the acute phase of such a condition the vision of 1 patient was reduced temporarily to perception of hand movements at 2 feet (60 cm.). Balyeat and Bowen,[5] in several of their cases, described a vesicular eruption, discrete or confluent, at the border of the cornea.

Involvement of the central part of the cornea at first was never as severe as that at the periphery, but as the latter process increased in severity the central portion of the cornea began to show deep and superficial edema and occasionally breaking down, due to lack of nutrition. This was seen to a rather remarkable degree in a patient hospitalized for slightly over seven weeks.

Rankine,[11] in a report of 1,598 cases of keratitis due to artificial silk poisoning, described three stages: (*a*) edema or irregular swelling of the corneal epithelium and actual pinhead elevations of the epithelium, (*b*) desquamation and (*c*) rapid and complete repair. The healing of the corneas in the 17 patients with keratitis in the present series was not as rapid as that described by Rankine, and in several with more serious disease it seemed to be influenced directly

10. Blank, P., Maj., M.C., A.U.S.: Personal communication to the author.

11. Rankine, D.: Artificial Silk Keratitis, Brit. M. J. **2**:6-9 (July 4) 1936.

by the response to allergic desensitization. Vascularization from the conjunctiva was an important factor in the healing of ulcers near the limbus.

Differential Diagnosis.—The following conditions, with the characteristic features indicated, may be differentiated from acute allergic conjunctivitis:

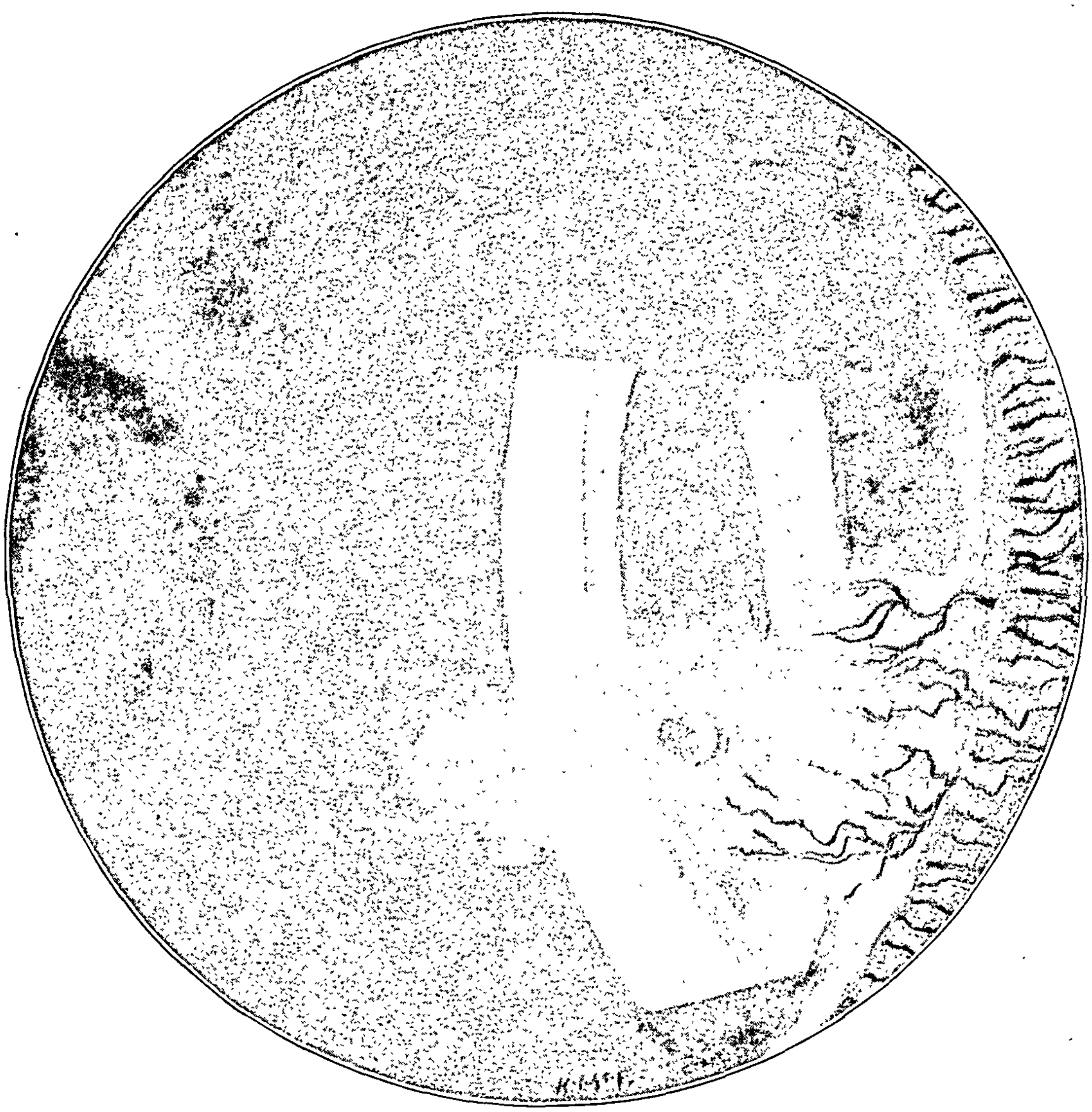
Acute Catarrhal Conjunctivitis: Usual presence of the causative organism in cultures and smears, more purulent exudate (as a rule) and frequent infection of the upper respiratory tract.

Acute Follicular Conjunctivitis of Beál: Rapid onset, complete resolution, presence of follicles, epidemic qualities and preauricular adenopathy.

Swimming Pool Conjunctivitis: Presence of many conjunctival follicles and of inclusion bodies, history of possible contact or epidemic and response to sulfonamide compounds administered locally and/or by mouth.

The following diseases, with the characteristics noted, can be differentiated from chronic allergic conjunctivitis:

Trachoma: Characteristic involvement of the upper lid, presence of Prowazek inclusion bodies, evidence on examination with the slit lamp of superficial pannus formation on the superior part of the cornea and, usually, a history of residence in the tropics or association with a trachomatous district.



Biomicroscopic view of the cornea and iris with a wide slit beam, showing the primary site of the allergic ulcer, with secondary extension of the infiltration toward the limbus, and corneal vascularization from the conjunctiva, an indication of early healing.

Parinaud's Syndrome: Sporothrix or Leptothrix in smears and cultures, and presence of preauricular adenopathy and chronic conjunctival granulations, which persist despite treatment.

Chronic Catarrhal Conjunctivitis: Presence of chronic infection of the tear sac, poor mechanical action of the lids, constant exposure to irritating chemicals or light rays, presence of dermatologic lesions on the lids or face, chronic involvement of the meibomian glands and possible

THE CORNEA

VI. PERMEABILITY CHARACTERISTICS OF THE EXCISED CORNEA

DAVID G. COGAN, M.D.; ERWIN O. HIRSCH, B.A., AND
V. EVERETT KINSEY, PH.D.
BOSTON

While comprehensive investigations of corneal permeability have been few, numerous isolated observations, employing a variety of technics and test substances and leading to diverse conclusions, have been reported. The subject was reviewed in 1937 by Grönvall [1]; since this time 2 additional reports have appeared.[2]

Until recently there has been wide acceptance of Leber's thesis that the epithelium and endothelium were impermeable to water, since the corneal stroma did not appear to imbibe fluid from the tears or the aqueous. At the same time, these membranes have been thought to be permeable to various dissolved substances, notably, the drugs commonly used in ophthalmologic practice. In recent times, Fischer [3] claimed to have shown that the cornea possesses a unidirectional permeability, similar to that previously hypothesized by Wertheimer for frog skin. According to Fischer's interpretation, water, sodium chloride, oxygen, alkaloids and acid dyes pass through the cornea from without inward, while carbon dioxide, and probably basic dyes, penetrate in the opposite direction. Cogan and Kinsey,[2a] on the other hand, observed that the epithelium and endothelium of the excised cornea were practically impermeable to the passage of chlorides in either direction and were freely permeable to the passage of water in both directions. The corneal stroma was freely permeable both to chlorides and to water. These authors pointed out that this permeability was not only compatible with, but actually accounted for, the maintained deturgescent state of the corneal stroma. Swan and White [2b] measured the penetration of various substances into the cornea and found, in confirmation of Höber's observations on the amphibian kidney, that penetration did not take place by simple diffusion, so far as it did not vary with molecular size but, rather, occurred in inverse relation to the degree of polarity of the molecule.

It is our present purpose to report the permeability of the excised cornea to a series of test substances, with the aim of determining whether the barrier properties of the epithelium were (1) indiscriminate, that is, present for all substances which did not actually destroy the membrane; (2) dependent on charge, that is, different for anions, cations and nonelectrolytes; (3) dependent on molecular size, or (4) dependent on lipid-water solubility. Appropriate substances were selected on the basis of availability, the ease with which quantitative determinations could be made and the absence of toxic effects on the cornea.

The method employed for measuring the penetration of the cornea by various substances was essentially the same as that previously described for sodium chloride.[2a] Freshly excised beef corneas were tied onto the flared lower ends of graduated glass tubes. The tubes were partly filled with the test solutions and the lower ends immersed in a flask of suitable fluid. The amount of test substance which had penetrated from the tube into the flask was determined after an arbitrary period of eighteen hours. All experiments were run in triplicate at least. This was found to give sufficient information for classification of the substances according to their penetration of the cornea. It was not intended to obtain the mass of data that would be necessary for rigorous quantitative comparison of the individual substances.

The corneas were excised whole or after removal of the epithelium. As has previously been noted, this technic is suitable for study of the permeability only of the epithelium-stroma combination or of the stroma alone, since the endothelium is invariably removed by the manipulation and Descemet's membrane may be considered, with respect to its permeability characteristics,

From the Howe Laboratory of Ophthalmology, Harvard Medical School.

1. Grönvall, H.: Citric Acid Studies Referring to the Eye, Acta ophth., 1937, supp. 14, pp. 1-279.

2. (*a*) Cogan, D. G., and Kinsey, V. E.: The Cornea: I. Transfer of Water and Sodium Chloride by Osmosis and Diffusion Through the Excised Cornea, Arch. Ophth. **27**:466-476 (March) 1942. (*b*) Swan, K. C., and White, N. G.: Corneal Permeability: I. Factors Affecting Penetration of Drugs into the Cornea, Am. J. Ophth. **25**:1043-1058, 1942.

3. Fischer, F. P.: Untersuchungen über Quellungsvorgänge und über Permeabilitätsverhältnisse der Hornhaut, Arch. f. Augenh. **98**:41, 1928; Ueber die Permeabilität der Hornhaut und über Vitalfärbungen des vorderen Bulbusabschnittes mit Bemerkungen über die Vitalfärbung des Plexus chorioideus, ibid. **100-101**: 480, 1929.

as a part of the stroma. The cornea was tied on the tube with the epithelial, or outer, side of the cornea toward the lumen. The transfer of test substance, unless otherwise indicated, was in the direction anterior to the posterior surface of the cornea. The area of the cornea exposed to the lumen of the tube was approximately 0.4 sq. cm.

One cubic centimeter of the test solution was placed in the tube. The concentration used differed for the various test substances. The solutions were not stirred during the test period. The fluid in the tube was hypertonic to that in the flask by at least 0.2 mol of sodium chloride, or its osmotic equivalent. Sodium chloride was added to the test solutions when necessary to make the solutions hypertonic. All solutions had a hydrogen ion concentration of approximately p_H 7.

Water was used as the fluid in the flasks in all experiments except those involving purely fat-soluble substances. Cyclohexane (hexamethylene) was used in experiments employing tributyrin, vitamin A and sudan IV, and purified kerosene, in the experiments involving carbon disulfide.

At the end of the eighteen hour test period the fluid in the flask was removed and analyzed for the amount of test substance which had been transferred. The results were corrected for blanks obtained from the experiments similarly conducted but without the test substance. When it was thought that considerable absorption or destruction of the test substance within the cornea might have taken place, the amount of test substance remaining in the tube after the experiment was also determined.

Finally, the cornea was checked for epithelial damage in instances in which the epithelium was supposed to be intact and, conversely, for the adequacy of the removal of epithelium in the instances in which the stroma only was being studied. This was checked either by testing the transfer of sodium chloride concomitantly with that of the test substance or by testing the transfer of fluorescein at the conclusion of the experiment. Normally, the epithelium is an effective barrier to sodium chloride and to fluorescein in 1.5 per cent solution of sodium chloride. When any appreciable amount of these substances was transferred under the aforedescribed experimental conditions, the epithelium was presumed to be damaged, and the results obtained with these substances were not included in the present series.

On the basis of their permeability through the cornea, the substances tested are readily classified. They characteristically fall into one of the following groups: (1) substances which pass through the stroma to a much greater degree than through the epithelium-stroma combination (table 1); (2) substances which pass through the stroma and the epithelium-stroma combination to not greatly different degrees (table 2), and (3) substances which do not pass through either the stroma or the epithelium-stroma combination (table 3). The data in these tables are self explanatory.

To determine whether or not the barrier properties of the epithelium-stroma combination were unidirectional, the permeability of the cornea was tested for passage in both directions of a number of the substances listed in table 1 by reversal of the corneal surfaces on the tube. The electrolytes so tested were chloride, bromide, iron (ferric ion), thiocyanate and phosphate, and the nonelectrolytes were urea, levulose and inulin. No difference in corneal permeability was found to transfer of substances in the two directions.

In the light of Michaelis'[4] observation that some membranes (apple skin, parchment paper and collodion) which showed an apparent impermeability to all ions dialyzed against water were permeable to cations dialyzed against a solution of sodium chloride, the permeability of the cornea to calcium (calcium chloride), to iron (ferric sulfate) and to bromide (sodium bromide) was measured, both water and solutions of sodium chloride being used in the flasks. The epithelium-stroma combination remained practically impermeable to cations and anions irrespective of the presence of sodium chloride in the flask. However, it was observed that in the absence of the epithelium less chloride was transferred in eighteen hours from tubes containing a molar solution of sodium chloride into flasks containing a molar solution of sodium nitrate than into flasks containing water (an amount equivalent to 30 mg. of sodium chloride in the former and to 50 mg. in the latter).[5]

For comparative purposes, the permeability of the conjunctiva and sclera was tested with some of the substances. The technic was similar to that employed in testing the permeability of the cornea. The sclera, with or without the conjunctiva, was tied onto the tube, with the conjunctival surface facing the lumen. In order to maintain the conjunctival-scleral relations as nearly normal as possible, the portions selected for study were those adjacent to the limbus. It should be noted, however, that the sclera of the beef eye is considerably thicker in this region than is the stroma of the cornea. The substances tested were chlorides, phosphates, levulose, alpha-naphthylamine, aniline, methylene blue (methylthionine chloride), hematoxylin, orange G, amaranth, orange I, light green SF yellowish, eosin and fluorescein. Somewhat less of the test substance was transferred through the sclera in eighteen hours than through the corneal stroma, owing to the greater thickness of the sclera,[6] while the amount transferred through the conjunctiva-sclera combination was somewhat greater than that transferred through the epithelium and stroma of the cornea. Nevertheless, the conjunctiva-sclera combination was a selective barrier to the same group of substances as was the epithelium-stroma combination of the cornea, albeit less effective.

In the corneal experiments listed in tables 1 and 2, water was transferred from the flask into the tube, as would be expected on the basis of osmosis, so long as the epithelium was present and acted as a barrier to the test substances. However, unlike the experiments in table 1, in which the amount of transfer was proportional to the degree of hypertonicity of the fluid in the tube, the substances listed in table 2 appeared partially to "block" the transfer of water through the epithelium. Thus, less water was transferred into the tubes which contained both test substance and solution of sodium

4. Michaelis, L.: Theory of Permeability of Membranes for Electrolytes, J. Gen. Physiol. 8:33, 1925.

5. This difference was also observed in the transfer of chlorides from a molar solution of potassium chloride in the tubes, but not from a molar solution of calcium chloride, into flasks containing water and a molar solution of sodium nitrate.

6. When thinner portions of the sclera were used, such as sections from the posterior pole of the eye, there was no significant difference in the amount transferred.

TABLE 1.—*Substances Which Pass Through the Stroma to a Much Greater Degree Than Through the Epithelium-Stroma Combination*

Test Substance	Initial Concentration in Tube, Mg./Cc.	Per Cent of Total Transferred in 18 Hours: Epithelium and Stroma	Stroma Only	Analytic Test
Br^-(NaBr)	15.0	1	70	Wuth, O.: J. A. M. A. **88**: 2013 (June 25) 1927
Cl^-(NaCl)	15.0	0	70	Fajans, K.: Ztschr. f. phys. Chem. **97**: 478-502, 1921
Cl^-(NaCl)	50.0	0	70	Fajans, K.: Ztschr. f. phys. Chem. **97**: 478-502, 1921
P(Na_2HPO_4 & KH_2PO_4 Buffer) p_H 7	2.0	0.9	55	Fiske, C. H., and Subbarow, Y.: J. Biol. Chem. **66**: 375, 1925
SCN^-(NaSCN)	13.7	1	93	Snell, F. D., and Snell, C. T.: Colorimetric Methods of Analysis, ed. 2, New York, D. Van Nostrand Company, Inc., 1936, vol. 1, p. 608
Fe^{++}($FeSO_4$)	50.0	<0.01	50	Snell and Snell, p. 300
Fe^{+++}($FeCl_3$)	50.0	<0.25	2	Snell and Snell, p. 300
Ca^{++}($CaCl_2$)	111.0	<1	25.3	Clark and Collip, in Todd, J. C., and Sanford, A. H.: Clinical Diagnosis by Laboratory Methods, ed. 8, Philadelphia, W. B. Saunders Company, 1935, p. 378
Glycerin	100.0	2	48	Colorimetric: Reduction of $K_2Cr_2O_7$
Levulose	70.0	2	36	Corcoran, A. C., and Page, I. H.: J. Biol. Chem. **127**: 601, 1939
Inulin	10.0	<0.2	8	Corcoran, A. C., and Page, I. H.: J. Biol. Chem. **127**: 601, 1939
Urea	3.1	1.6	26	Folin, O.: Laboratory Manual of Biological Chemistry, ed. 5, New York, D. Appleton-Century Company, Inc., 1934, p. 149
Methylene blue	0.1	0	ca 25	Colorimetric
Fluorescein	1.0	0	ca 50	Colorimetric
Hematoxylin	5.0	0	ca 63	Colorimetric
New fuchsin	Saturated solution	0	ca 7	Colorimetric
8-sulfonic naphthylamine	2.5	1.8	38	Bratton, A. C., and Marshall, E. K., Jr.: J. Biol. Chem. **128**: 537, 1939

TABLE 2.—*Substances Which Pass Through the Stroma and the Epithelium-Stroma Combination in Not Greatly Different Degrees*

Test Substance	Initial Concentration in Tube	Per Cent of Total Transferred in 18 Hours: Epithelium and Stroma	Stroma Only	Analytic Test
6, 8-sulfonic naphthylamine	2.5 mg./cc.	<0.5	2.3	Bratton, A. C., and Marshall, E. K., Jr.: J. Biol. Chem. **128**: 537, 1939
α-naphthylamine	1.7 mg./cc.	1.0	2.0	Bratton, A. C., and Marshall, E. K., Jr.: J. Biol. Chem. **128**: 537, 1939
Aniline	2.5 mg./cc.	30	60	Snell, F. D., and Snell, C. T.: Colorimetric Methods of Analysis, New York, D. Van Nostrand Company, Inc., 1936, vol. 2, p. 408
Glyceryl triacetate, 100%	100%	5	10	Colorimetric: Reduction of $K_2Cr_2O_7$
Glyceryl triacetate, 5%	5%	20	40	Colorimetric: Reduction of $K_2Cr_2O_7$
Alcohol (ethyl)	10%	35	50	Colorimetric: Reduction of $K_2Cr_2O_7$
Thiodiglycol, 100%	100%	3	10	Colorimetric: Reduction of $K_2Cr_2O_7$
Thiodiglycol, 5%	5%	8.5	53	Colorimetric: Reduction of $K_2Cr_2O_7$
Acetone	5%	10	34	Folin, O.: Laboratory Manual of Biological Chemistry, ed. 5, New York, D. Appleton-Century Company, Inc., 1934, p. 205

TABLE 3.—*Substances Which Do Not Pass Through Either the Stroma or the Epithelium-Stroma Combination*

Test Substance	Initial Concentration in Tube	Per Cent of Total Transferred in 18 Hours: Epithelium and Stroma	Stroma Only	Analytic Test
Serum protein	70 mg./cc. in water	0	0	Nephelometric
Congo red	0.5:100 in water	0	0	Colorimetric
Sudan IV	About 1 mg./cc. in cyclohexane	0	0	Colorimetric
Glyceryl tributyrate	10% in cyclohexane	0	0	Colorimetric: Reduction of potassium bichromate
Carbon disulfide, 5%	5% in kerosene	Damaged epithelium	0	Bell and Agruss: Indust. & Engin. Chem. **13**: 297, 1941
Vitamin A as halibut liver oil	740 U. S. P. units of vitamin A per cc. of halibut liver oil	0.5	0.5	Snell, F. D., and Snell, C. T.: Colorimetric Methods of Analysis, New York, D. Van Nostrand Company, Inc., 1936, vol. 2, p. 617

chloride than when equivalent concentrations of a solution of sodium chloride only were present. Indeed, in the presence of pure glyceryl triacetate and pure thiodiglycol, practically no water passed into the tube during the eighteen hours of the experiments so long as the epithelium was intact (0.07 cc. and 0 respectively), while considerable water was transferred into the tube when the epithelium was removed (0.14 and 0.23 cc. respectively). This blockage was reversible, since subsequent substitution for the test substance in the tube of the standard solution of sodium chloride showed that the corneas with intact epithelium possessed their normal degree of semipermeability. Our tentative explanation for this phenomenon is that the substances in table 2, being soluble in lipids, were absorbed into the epithelium[7] and formed a lipid barrier to the transfer of water. This does not occur in the absence of the epithelium.[8]

Since the cornea is permeable to some substances and not to others, several mechanisms of selectivity may be considered. In keeping with current theses of permeability, the cornea might be considered a membrane with sievelike properties determining the passage of substances by molecular size, or as a membrane with electrostatic properties permitting the passage of certain substances on the basis of charge or absence of charge, or, finally, as a membrane containing a solvent, or a series of solvents permitting the passage of such substances as possess the appropriate solubilities.

Obviously, corneal permeability cannot be accounted for solely by the pore theory, since the molecular sizes of the substances listed in table 2, which penetrate the epithelium-stroma combination, are considerably greater than those of many of the nonpenetrating substances listed in table 1. Nevertheless, penetration of various acid dyes through the isolated stroma appeared to be in the approximate order of the sizes of their particles (table 4).

As for the electrostatic hypothesis, it is true that electrolytes were uniformly retained by the epithelium, but so were many nonelectrolytes. Moreover, no exchange of ions occurred when different salts were present on each side of the cornea. Hence, charge or absence of charge cannot alone account for the differential permeability.

The one difference which is obvious in the substances of tables 1, 2 and 3 is their variation in solubilities. The test agents listed in table 1, which characteristically pass through the stroma but not the epithelium, are substances that are predominantly nonsoluble in fats.[9] The test agents listed in table 2, which pass through both the epithelium and the stroma, are substances that are characteristically soluble in both water and fat. The substances listed in table 3, which do not pass through the stroma or the epithelium-stroma combination, are substances that either have very large molecules (proteins and congo red) or are insoluble in water. Whether or not the test substances of table 3 penetrated the epithelium could not be determined with the present technic.

In consideration of the foregoing results, it is concluded that transfer through the cornea is largely a matter of phase solubility. Specifically, the epithelium is believed to be permeable to substances with a fat-soluble phase.[10] and the stroma to substances with a water-soluble phase. However, water itself is an exception, for it passes through the epithelium.[11] (While no comprehensive experiments have been conducted on the selectivity of endothelial permeability, the results of experiments in vivo with chlorides, on the one hand, and with atropine and aniline,[12] on the other, are consistent with the thesis that the endothelium has the same properties of perme-

TABLE 4.—*Permeability of the Corneal Stroma to Various Dyes, Related to Size of Particles**

Test Substance	Approximate Percentage of Total Transferred Through Stroma in 18 Hr.†	Approximate Size of Particle ‡
Orange G	100	4.0 ± 0.4
Eosin	25	5.3 ± 0.5
Orange I	10	5.0 ± 0.3
Amaranth	10	6.1 ± 0.3
Light green S. F. yellowish	2.5	6.6 ± 0.4
Congo red	0	13.2 ± 0.8

* The initial concentration in the tubes was 5 mg. per cubic centimeter in all cases.

† None was transferred through the epithelium-stroma combination.

‡ From Gordon, H. K., and Chambers, R.: Particle Size of Acid Dyes and Their Diffusability into Living Cells, J. Cell. & Comp. Physiol. **17**: 97-108, 1941.

7. The fat content of the corneal epithelium is 10 per cent of its dry weight, as compared with 1 per cent of the dry weight of the stroma (Krause, A. C.: Biochemistry of the Eye, Johns Hopkins Press, 1934).

8. This result is consistent with the observations of Swan and White that some of the naphthylamines are taken up by the cornea most readily when the epithelium is present.

9. Glycerin is ordinarily considered to be soluble in lipids because of its solubility in the common organic solvents, but its solubility in fats, such as glyceryl trioleate and glyceryl tributyrate, is actually slight.

10. It is to be noted that the actual fat of the corneal epithelium which is responsible for the permeability properties is not known.

11. The paradox of water transfer through lipid membranes is what led Nathanson (J. Botan. **39**:607, 1904) to postulate his theory of mosaic distribution of the lipid elements on cell surfaces.

12. A report of this work is to be published subsequently.

ability as the epithelium.) For a substance to pass through the intact cornea it is essential, therefore, that it have biphasic solubilities.

The application of these observations to the practical matter of transfer of alkaloids through the intact cornea in vitro and in vivo will be discussed in a separate communication.

SUMMARY AND CONCLUSIONS

In a study of the permeability of the excised cornea to a variety of substances it was observed that purely water-soluble substances do not pass through the epithelium (nor, in all probability, through the endothelium), while purely fat-soluble substances do not pass through the stroma. With the exception of water, substances which do get through the whole cornea have characteristically biphasic solubilities. Transfer of substances across the excised cornea does not differ appreciably in the two directions. The conjunctiva has properties of permeability that are qualitatively similar to those of the corneal epithelium, but less rigorous, and the sclera has properties similar to those of the corneal stroma.

Howe Laboratory of Ophthalmology.

EXPERIMENTAL STUDIES OF OCULAR TUBERCULOSIS

VIII. A STUDY OF THE INCREASED RESISTANCE TO REINOCULATION AFTER RECOVERY FROM OCULAR TUBERCULOSIS SHOWN BY THE IMMUNE-ALLERGIC RABBIT

ALAN C. WOODS, M.D., AND EARL L. BURKY, M.D.

BALTIMORE

In a previous study [1] it was noted that for an undetermined period after recovery from an attack of secondary ocular tuberculosis the previously diseased eyes were endowed with a relative immunity to reinoculation with tubercle bacilli. When such eyes were given an inoculation of tubercle bacilli which produced typical disease in the normal fellow eye, the recovered eyes showed only a transient reaction to the tuberculin in the inoculum and did not have a second attack of tuberculosis. The studies at that time indicated that this local resistance was not due either to an increase in the general systemic immunity or to an exhaustion of the reaction capacity of the eye. It appeared to be related to some local condition in the eye itself. The purpose of this paper is to report further studies on this phenomenon of increased local resistance.

These studies are reported in two parts. The first part consists of an experiment dealing with (1) the relation of vascularity to the apparent local increased resistance and (2) the duration of the apparent local increased resistance. The second part consists of a series of clinical and histologic observations concerned with the relation of the increased resistance to the presence of an active, though clinically unrecognized, focus of tuberculosis in the eyes.

EXPERIMENTAL STUDY

Studies already reported [1] showed that the lack of reaction to a second injection of tubercle bacilli was not due to a decrease in the general reaction capacity of such eyes. The recovered eyes showed pronounced reaction to tuberculin in the inoculum and reacted in characteristic manner to inoculation with Brucella organisms. The possibility that the apparent immunity was due to an exhaustion of the reaction capacity of the eyes was therefore dismissed. In the following experiment attention was centered on the possible relation of local increased vascularization to the local resistant state and on the duration of the apparent local immunity.

PLAN OF EXPERIMENT

The object of this experiment was to investigate the question: Is the vascularization resulting from the previous attack of ocular tuberculosis concerned in the increased resistance? To this end, in immune-allergic rabbits, a comparison was made of the reaction to inoculation in eyes with tuberculous vascularization and that in eyes with nontuberculous vascularization. To accomplish this, two groups of immune-allergic rabbits were prepared.

Group A: This was a group of immune-allergic rabbits which had recovered from an attack of ocular tuberculosis in one eye. These rabbits had been inoculated in the right eye with the usual dose of tubercle bacilli, and the resulting ocular disease had been allowed to run its course. At the beginning of the experiment these eyes were scarred and vascularized, but the disease had been clinically inactive for an average period of six weeks. A previous study [1] had shown that the resistance to reinoculation endured for at least this period.

Group B: This group consisted of immune-allergic rabbits with nontuberculous vascularization of one eye. They were prepared in the following manner: A series of immune-allergic rabbits were inoculated in the right eyes with either living Brucella organisms or Listerella monocytogenes. Since these organisms produced an irregular degree of vascularization, all the rabbits were given an additional intracorneal injection of killed staphylococci. The inflammatory symptoms and disease produced by these injections were allowed to subside. There resulted a clinically inactive condition, with conspicuous vascularization of the cornea and visibly dilated capillaries in the iris.

Group C: As controls, immune-allergic rabbits which had received no previous ocular injections were used. As additional controls, normal rabbits were inoculated in the eyes.

Before the test inoculations were made, specimen rabbits from groups A and B were killed and their eyes examined histologically to determine whether the degrees of vascularization in the eyes of the two groups were comparable. In general, the eyes of the rabbits in group B showed slightly more secondary vascularization than did the eyes of the rabbits in group A. In the rabbits in group B the inflammatory reaction had almost completely subsided, and there was little, if any, cellular infiltration.

Representatives of these three groups (A, B and C) and the normal controls were inoculated in both eyes

From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital.

1. Woods, A. C., and Burky, E. L.: Experimental Studies of Ocular Tuberculosis: VI. The Effect of Sensitivity and Immunity on the Experimental Lesions of Ocular Tuberculosis, Arch. Ophth. **25**:62-74 (Jan.) 1941.

at two week intervals, from Nov. 22, 1940 until March 3, 1941. Each subgroup so inoculated consisted of 2 rabbits from group A (immune-allergic rabbits with clinically healed tuberculous uveitis in one eye), 3 rabbits from group B (immune-allergic rabbits with nontuberculous scarring and vascularization of one eye), 1 rabbit from group C (immune-allergic rabbits with normal eyes) and 1 normal rabbit. The inoculations were made in the anterior chamber with the usual dose of 0.25 cc. of the undiluted paper filtrate of a six week culture of the virulent human tubercle bacillus used in these experiments.

A comparison of the course and intensity of any resulting tuberculous disease in the various eyes inoculated permitted an estimate of the influence of the following factors: *A*. The effect of scarring and vascularization in themselves on the tuberculous lesion. This could be estimated by comparing any tuberculous disease in the right eyes of the rabbits in group A (tuberculous scarring and vascularization) with the tuberculous disease in the right eyes of the rabbits in group B (nontuberculous scarring and vascularization) and with the disease in the left eyes (previously normal) of these same rabbits. The course of the disease in the rabbits in group C (immune-allergic rabbits with previously normal eyes) acted as a control for these observations. *B*. The presence and duration of any increased local resistance in the recovered eyes. This was determined by the occurrence of any disease in the right (previously diseased) eyes and the left (previously normal) eyes of the rabbits in group A, the inoculated eyes of the rabbits in group C acting as controls. The reaction in the eyes of the normal rabbits acted as a further control for the activity and virulence of the inoculum. Since all these normal rabbits showed the usual reaction of delayed inflammation, with caseation and, usually, perforation, they will not be mentioned further.

The eight subgroups were inoculated in the manner described, at two week intervals. After inoculation each subgroup was kept under observation for a further period of sixteen weeks. The eyes of all rabbits were examined clinically each week, the degree of ciliary congestion, new vascularization and infiltration of the cornea, the presence of tubercles and inflammatory process in the iris and of cells in the aqueous and evidences of caseation and necrosis being recorded on a numerical scale. An estimate of the total activity in each individual eye was then made. These estimates were averaged and plotted on coordinate paper. The resulting curves showed the course of the disease followed by the various eyes over the period of observation. Thus, in figure 1 (which is shown as a specimen of the curves for each subgroup), curve *A* represents the course of the tuberculous disease in the formerly tuberculous right eyes of the rabbits in group A; curve A^1, the average course of the disease in the previously undiseased left eyes of the rabbits in group A; curve *B*, the average course in the nontuberculous vascularized and scarred right eyes of the rabbits in group B and curve B^1, the course in the previously normal left eyes of the same rabbits. Curve *C* represents the average course of the disease in both the right and the left eye of the rabbits in group C, and curve *D*, the average course in the right and the left eye of the normal control rabbits.

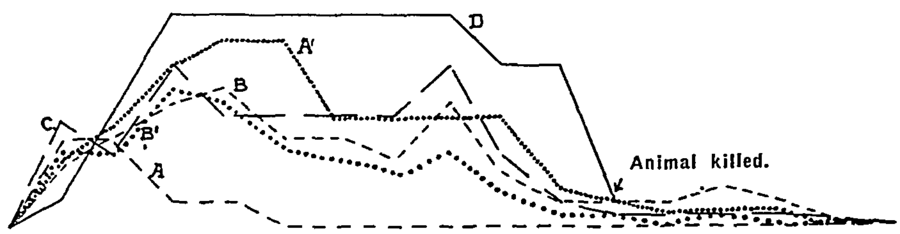


Fig. 1.—Course of tuberculous ocular disease in specimen subgroups of rabbits.

Curve *A* represents the sensitivity of the right eye (tuberculous vascularization) of rabbits in group A; curve A^1, that of the left eye (previously normal) of rabbits in group A; curve *B*, that of the right eye (nontuberculous vascularization) of rabbits in group B; curve B^1, that of the left eye (previously normal) of rabbits in group B; curve *C*, that of both eyes (previously normal) of immune-allergic control rabbits, and curve *D*, that of eyes of normal control rabbits.

EXPERIMENTAL RESULTS

1. *Relation of Local Vascularization to Local Resistance*.—The increased vascularization in the eyes of the immune-allergic rabbits in group B did not result in any increased resistance to subsequent inoculation with tubercle bacilli in any of the eight subgroups. In all the nontuberculous vascularized right eyes and the previously normal left eyes of the immune-allergic rabbits of group B there developed a definite and typical ocular tuberculosis of similar intensity. In general, the severity of the tuberculous reactions in the rabbits in group B was slightly less than that shown by the control immune-allergic rabbits in group C. This difference, however, was within the range of variations shown by some other groups of immune-allergic rabbits. The degree of ocular tuberculosis resulting in the right eyes of the rabbits in group B was definitely greater than anything manifested by the rabbits in group A, in which the vascularization and scarring were the results of former ocular tuberculosis. It is clear, therefore, since more severe reactions developed in the highly vascularized eyes of the rabbits in group B than in the eyes of the rabbits in group A, that vascularization in itself was not responsible for the relative resistance to reinoculation shown by the rabbits in group A. Indeed, it appears quite possible that the increased vascularity of the eyes of the rabbits in group B may have predisposed them to an increased inflammatory reaction.

2. *Duration of Apparent Resistance to Reinoculation*.—In study VI [1] it was reported that for at least six weeks after apparent clinical recovery from an attack of ocular tuberculosis the recov-

ered eyes were resistant to the usual reinoculation. This was the maximum period of observation in this study. In the experiment just reported the period of observation varied from six to twenty weeks after apparent recovery, i. e., from the time the first subgroup was inoculated, on Nov. 22, 1940, until the last subgroup was inoculated, on March 3, 1941.

The right eyes of the rabbits of the first five subgroups of group A, inoculated every two weeks from Nov. 22, 1940 to Jan. 18, 1941, showed a definite resistance to reinoculation. After the local reaction to the tuberculin in the inoculum subsided, the right (previously diseased) eyes showed little further reaction, while in the previously normal left eyes there developed the usual ocular tuberculosis exhibited by other immune-allergic rabbits when similarly inoculated. This is shown in figure 2, which is a composite curve for the first five subgroups. In this figure, curve *A* represents the average for the reactions of the right (previously diseased) eyes of the rabbits in group A; curve *B*, the average course of the lesion in the previously undiseased eyes of the various other immune-allergic rabbits, and curve *C*, the average course of the disease in the normal control rabbits.

The right eyes of the rabbits in the last three subgroups in group A, inoculated February 3 and 17 and March 3, failed to show complete immunity to reinoculation. After the subsidence of the initial reaction to the tuberculin in the inoculum, there developed in the right eyes of the rabbits of these three subgroups a low grade, but clinically recognizable, ocular tuberculosis of gradually increasing severity. The resistance of

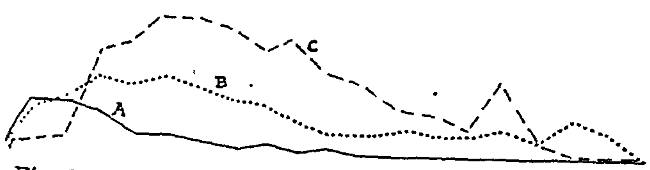


Fig. 2.—Composite chart for subgroups 1, 2, 3, 4 and 5. Curve *A* represents the average sensitivity to tuberculin of the right, tuberculous, eyes of group A rabbits; curve *B*, the average for the previously normal eyes of other immune-allergic rabbits, and curve *C*, the average for the normal eyes.

these eyes to reinoculation had diminished. Figure 3 shows the averages for the reactions in the last three subgroups. While the disease in these right eyes was less than in the controls, nevertheless, by the fifth week after inoculation of these eyes the tuberculous activity in the previously diseased eyes was nearly equal to that shown in the eyes of the other immune-allergic rabbits with no previous ocular tuberculosis.

The duration of the resistance to reinoculation was further tested by reinoculation of the eyes of immune-allergic rabbits in which the ocular disease had been inactive for one year. Study VII,[2] on the effect of desensitization on the ocular lesions, was terminated in May 1942. In May 1943, 32 rabbits survived from the experiment, and 14 of these were clinically free from any evidence of tuberculous inflammation in the eyes. The anterior chambers of both eyes of these 14 rabbits were then reinoculated. The reaction shown by the previously diseased right eyes and that shown by the previously normal left eyes of these rabbits were practically identical. In both eyes of all rabbits tuberculosis of about equal severity developed.

Fig. 3.—Composite chart for subgroups 6, 7 and 8. Curve *A* represents the average sensitivity to tuberculin of the right, tuberculous, eyes of group A rabbits; curve *B*, the average for previously normal eyes of other immune-allergic rabbits, and curve *C*, the average for the normal eyes.

It is evident, therefore, that resistance to reinoculation with tubercle bacilli manifested by eyes which have apparently recovered from an attack of tuberculosis, and which clinically appear inactive, is only transient. At best it lasts only about four months. After an interval of about this length, the eyes again become susceptible to reinoculation, and after a year there remains no vestige of any resistance to secondary reinoculation with tubercle bacilli.

CLINICAL AND HISTOLOGIC OBSERVATIONS

It was now clear that this transient resistance to reinoculation was not related (*a*) to a general immunity produced by the original systemic injection and enhanced by the secondary ocular injection (study VI), (*b*) to an exhaustion of the reaction capacity of the eye (study VI) or (*c*) to the increased vascularization resulting from the previous ocular disease. Therefore, to explore further the reason for this transient resistance to reinoculation, clinical analyses and histologic examinations were made.

In the interpretation of the results of inoculation experiments certain facts on the clinical course of experimental ocular tuberculosis should be kept clearly in mind. In this paper, and in previous papers of this series, the terms

2. Woods, A. C., and Burky, E. L.: Experimental Studies of Ocular Tuberculosis: VII. Effect of Desensitization with Tuberculin in Experimental Ocular Tuberculosis, Arch. Ophth. **29**:369-379 (March) 1943.

"healed" and "clinically inactive" have been used almost as synonyms. These terms carry the following implications: Such "healed," or "inactive," eyes showed no clinical evidence of active disease. The pericorneal congestion had subsided. The corneas, though scarred and often partially vascularized, showed no active infiltrates. The irises manifested no evidence either of actual tubercles or of active inflammation. The pupils were often occluded by organized exudates, so that ophthalmoscopic examination was impossible. When such examination was possible, although there was often clouding of the anterior portion of the vitreous, due to organization, there were no fresh vitreous veils, and the fundi, when visible, showed no exudates. The aqueous rays were negative.

TABLE 1.—*Data on Thirty-Two Rabbits One Year After Study on Effect of Desensitization on Ocular Tuberculosis*

Status of Eyes May 1942		No. of Eyes	Course 1942-1943: Inactive Disease	Course 1942-1943: Recurrence	Status of Eyes May 1943: Healed	Status of Eyes May 1943: Actively Diseased or Ruptured
Clinically inactive disease	A	11	7	4	7	4
	B	6	6	0	6	0
Trace of inflammation	A	3	3	0	3	0
	B	4	3	1	3	1
Active disease	A	0	0	0	0	0
	B	8	0	8	0	8

What was the subsequent fate of these eyes with clinically inactive and healed tuberculosis? A number of such eyes in rabbits, remaining from study VII,[2] on the effect of desensitization on the ocular lesion, were available for further study. At the end of this experiment, in May 1942, there remained 36 rabbits in the group which was treated with tuberculin (group A). In 1 of these rabbits the disease was still active; in 4 rabbits there was a trace of smouldering activity, and in 31 rabbits the disease was clinically inactive or healed. Of the untreated rabbits of the control group (B) there were 37 survivors. In 8 of these rabbits the disease was still active, in 4 rabbits there was a trace of activity, and in 25 rabbits the disease was inactive. During the year following the termination of study VII the mortality was heavy, and by May 1943 there were only 32 survivors, all told—14 in group A and 18 in group B. In 17 of these 32 survivors the disease had been clinically inactive in May 1942; 7 rabbits had shown a trace of inflammation, and 8 had had active inflammation at that time. The subsequent fate of these 32 rabbits is shown in table 1.

A study of this table reveals that of 17 eyes which were clinically healed, 4 had undergone recurrences and ruptured, while 13 showed no recurrences and still were clinically inactive one year later. Of the 7 eyes which had a trace of inflammation, 1 still had active disease one year later, while the condition in 6 had progressed to clinical inactivity or healing. All the 8 eyes which still showed activity in 1942 were those of rabbits in group B. In every rabbit the disease had progressed, and the eyes were virtually destroyed by tuberculosis one year later. The fate of the rabbits with a trace of inflammation was not remarkable. The results for the rabbits in these two categories were statistically the same for both group A and group B and require no comment. In summary, of the 14 survivors in group A, the eyes of 10 were healed, and those of 4 had ruptured. In group B, of 18 survivors, the eyes of 9 were healed and those of 9 had ruptured. Therefore, even though treatment with tuberculin had been discontinued with the rabbits of group A, the final results were better than those for the rabbits of group B. However, further analysis of the behavior of the rabbits which had clinically inactive disease in 1942 is possibly of significance.

There were 17 rabbits in this category—11 in group A, which had been desensitized, and 6 in group B, which had received no tuberculin and in which the apparent healing was spontaneous. Of the 11 desensitized rabbits, 4 had recurrences of the ocular inflammation, while the eyes of 7 remained healed. Of the 6 rabbits which had inactive disease and had received no tuberculin, none had recurrences. Thus, while the incidence of primary clinical healing was much greater in the desensitized group when the administration of tuberculin was stopped, there was a return of the sensitivity, and with this an incidence of recurrence of ocular tuberculosis of 36 per cent. On the other hand, in the group with spontaneous cessation of the tuberculous inflammation there were no recurrences. In support of the statement that sensitivity returned in these rabbits after tuberculin was stopped are the results of comparison of the sensitivity manifested by these animals in May 1942 with that shown in May 1943. The results of these determinations of cutaneous sensitivity are shown in table 2.

TABLE 2.—*Changes in Sensitivity to Tuberculin in Desensitized Rabbits During One Year*

Rabbits	Cutaneous Sensitivity: May 1942	Cutaneous Sensitivity: May 1943	Ocular Sensitivity, Right Eye Previously Desensitized: May 1942	Ocular Sensitivity, Right Eye Previously Desensitized: May 1943	Ocular Sensitivity, Left Eye Previously Normal: May 1942	Ocular Sensitivity, Left Eye Previously Normal: May 1943
Desensitized rabbits (group A)	0.5 (—) (0.05 mg. P.P.D.)*	1.6 = (0.005 mg. P.P.D.)	0.36	0.6	0.27	0.6

* P.P.D. indicates purified protein derivative.

Thus in one year the cutaneous sensitivity increased from a reading of 0.5 to 0.05 mg. of purified protein derivative to that of 1.6 to 0.005 mg., three times the extent of the reaction to one-tenth the dose. The ocular sensitivity in the previously diseased right eye had increased from 0.36 to 0.6, and that in the normal left eye, from facts become obvious: 1. The resistance of recovered eyes to reinoculation is not related to general immunity, to exhaustion of the reaction capacity of the eyes or to vascularization. 2. This resistance is transient. In eyes which showed no spontaneous recurrence (the only eyes thus tested), the resistance begins to fade

Fig. 4.—(*A*) Diffuse cellular infiltration of the ciliary body, and (*B*) inflammatory changes in the iris, in clinically "quiet" eyes (immune-allergic rabbits with secondary ocular tuberculosis).

0.27 to 0.6. This is in line with the well known clinical observation that after desensitization is accomplished by administration of tuberculin, the injections must be continued; otherwise sensitivity will almost invariably recur, with the danger of recurrence of the ocular inflammation.

However this may be, as a result of the observations thus far made on resistance and recurrence in experimental ocular tuberculosis, three in four months and is gone completely in one year. 3. Apparent clinical recovery is not an index of true healing—a large percentage of eyes which show apparent healing may manifest recurrent and violent tuberculous inflammation.

The next point was to determine whether histologic study of these recovered eyes at various times after recovery or inoculation could throw any light on the question why some eyes were

resistant to reinoculation and some were not. To this end, eyes which had been clinically inactive for six weeks and were presumably susceptible to reinoculation were sectioned and studied. The salient observations were as follows: 1. Eyes sectioned six weeks after apparent clinical recovery still showed definite evidences of active tuberculous inflammation, with diffuse lymphocytic

This observation at once suggested that the increased resistance to reinoculation shown by recently recovered eyes might be due to the presence of an active, but clinically unrecognizable, focus, already present in the eyes—in short, to the premobilization of the factors of resistance, which had already controlled the original infection. Similarly, the susceptibility to reinoculation

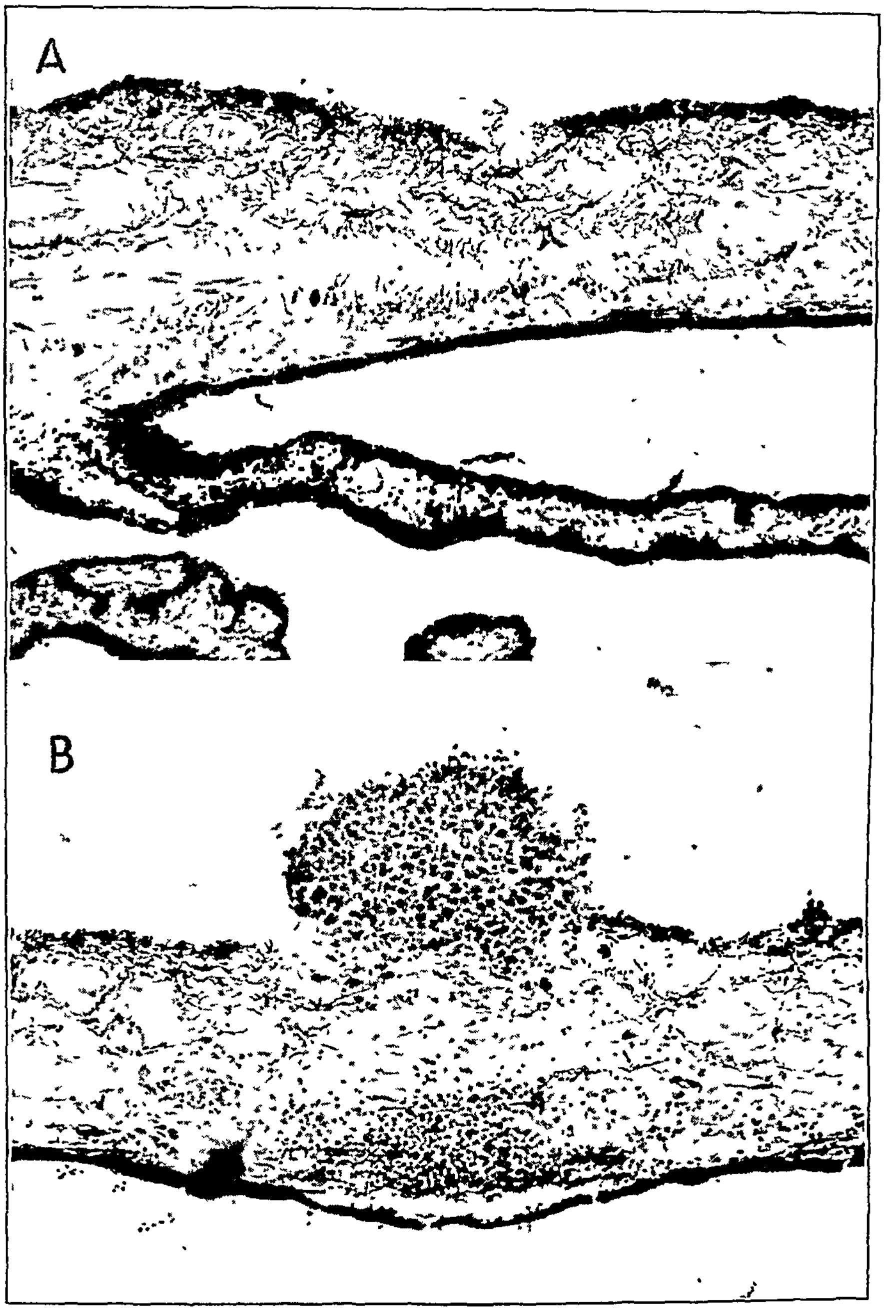


Fig. 5.—(*A*) Iris and ciliary body, and (*B*) early tubercle on the iris, eleven days after reinoculation in an immune-allergic rabbit with old healed secondary ocular tuberculosis. × 160.

infiltration, epithelioid cells and macrophages, often with deep, usually well encapsulated, tubercles (fig. 4 *A* and *B*). 2. Eyes sectioned one year after apparent clinical recovery, during which there had been no recurrences, showed heavy, nonspecific scarring but no active cellular infiltration or tubercules, such as were present in recently recovered eyes.

shown by eyes which had been clinically healed for a longer period might be due to the disappearance of these same factors of resistance—the macrophages and the epithelioid cells. Obviously, this proposition is not capable of absolute proof, for it is manifestly impossible to section an eye, demonstrate the presence or absence of active cellular infiltration and later reinoculate the same

ye to determine its resistant state. Group inculations, however, made this a plausible hypothsis—a group of apparently recovered eyes, specimens of which showed an active focus of tuberculosis with cellular infiltration, were resistant to reinoculation, while a group of eyes recovered for a longer period, specimens of which showed no active focus of tuberculosis and only slight cellular infiltration, were not resistant to reinoculation and a second attack of ocular tuberculosis developed on reinoculation with tubercle bacilli.

Further clinical and histologic examinations were made on 14 rabbits remaining from study VII[2] (immune-allergic rabbits with healed secondary ocular tuberculosis). This was done to determine whether these rabbits differed significantly from immune-allergic rabbits which had not undergone a previous attack of ocular tuberculosis with respect to the clinical course of a second attack of ocular tuberculosis and the histologic appearance of the eyes. These 14 rabbits were, therefore, reinoculated in the right eye, which had been the site of the former attack. Thereafter, at two week intervals after inoculation, sample pairs of animals were killed for histologic examination. Surviving rabbits were kept under constant clinical observation. These rabbits all showed a moderate initial reaction to the tuberculin in the inoculum. This usually faded within a week, and after a short latent period clinical symptoms of tuberculous

Fig. 6.—(*A*) Diffuse cellular infiltration of the iris, and (*B*) early tubercles of the cornea, nineteen days after reinoculation in immune-allergic rabbit with old healed secondary ocular tuberculosis. × 50.

inflammation developed. In the latter stages the disease tended to be more serious than is usually observed in immune-allergic rabbits, a few of the eyes showing caseation and necrosis and finally rupturing. In this respect the ocular disease simulated the picture observed in normal, nonimmune rabbits and was possibly an index of the degree to which the immunity had declined in the individual animals.

The first rabbit employed for histologic study was killed eleven days after reinoculation of the eyes. In this rabbit the reaction to the tuberculin in the inoculum had been relatively moderate and had completely subsided. Histologic study of this eye showed old scarring of the iris and ciliary body and a minimum of cellular infiltration (fig. 5 *A*). The one evidence of early disease was a small tubercle forming on the anterior surface of the iris (5 *B*). The next rabbits used were killed nineteen days after reinoculation of the eyes. These rabbits already showed clinical evidence of tuberculous inflammation. Histologically the eyes showed diffuse infiltration of the iris and ciliary body, with serous exudates and cells, including lymphocytes, leukocytes, epithelioid cells and large mononuclears (fig. 6 *A*), and beginning invasion of the cornea (fig. 6 *B*). Rabbits killed forty-five days after reinoculation showed more advanced disease, tubercles being present throughout the an-

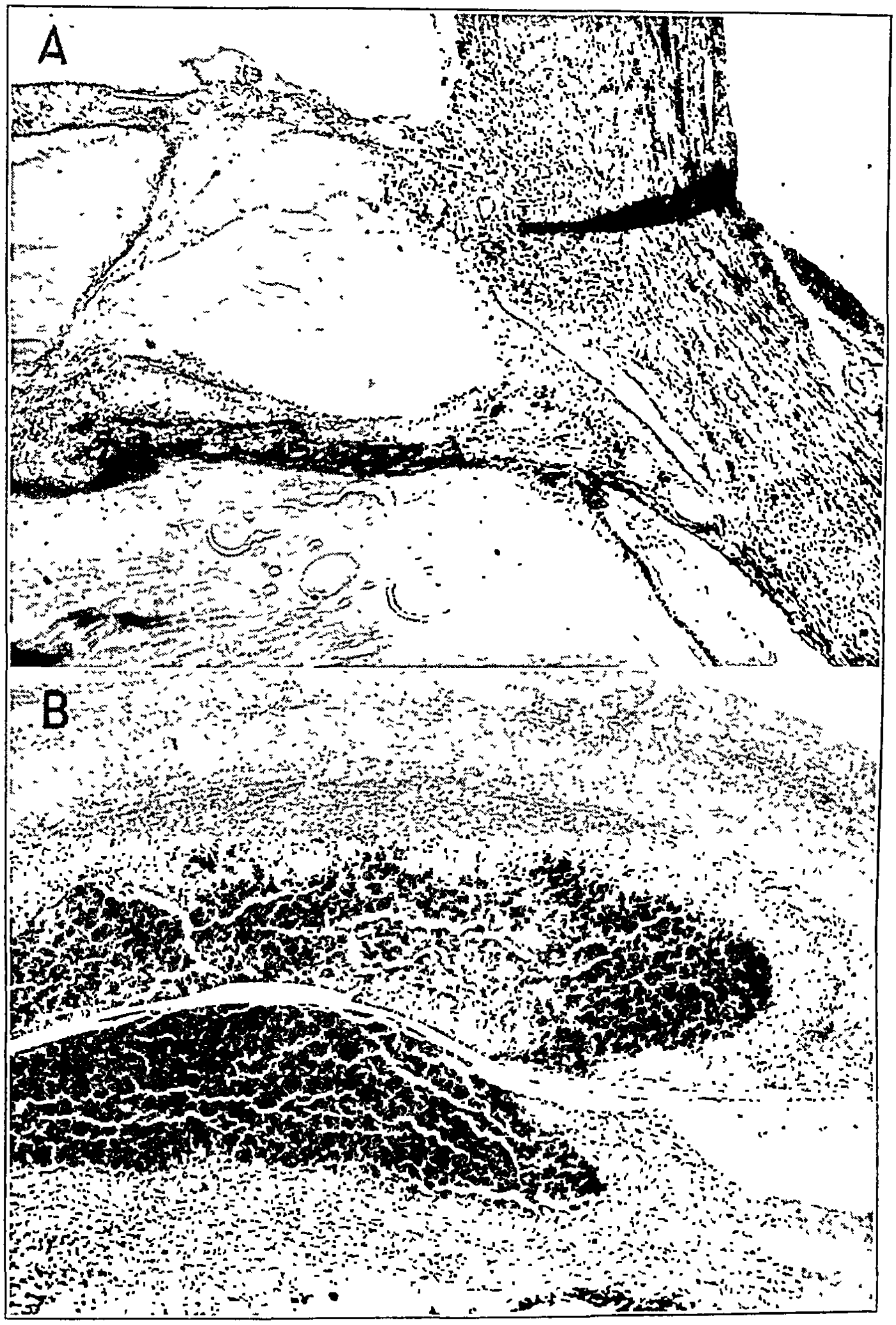


Fig. 7.—(*A*) Well marked tuberculosis of the iris, ciliary region and cornea, with early necrosis, forty-five days after reinoculation, and (*B*) large caseating tuberculoma of the cornea and the root of the iris seventy-seven days after reinoculation, in immune-allergic rabbits with old healed secondary ocular tuberculosis. × 50.

terior uveal tract and cornea, with early necrosis (fig. 7 *A*). Rabbits killed late in the experiment, seventy-seven days after reinoculation, showed advanced disease, with pronounced corneal involvement, caseation and necrosis. Figure 7 *B* shows a large necrotic, but somewhat atypical, tuberculoma, involving both the iris and the cornea at the angle of the anterior chamber.

COMMENT

The one positive result in these experiments is the observation that the resistance to reinoculation manifested by recently recovered eyes is a transitory phenomenon. It appears to be related to the presence of macrophagic cells in the ocular tissues. When the tuberculous foci become inactive, the cellular infiltration becomes less, and the eyes show only what might be called "nonspecific scarring;" then the resistance to reinoculation vanishes. Since one can apparently rule out other obvious factors, it appears logical to conclude that the resistance shown to reinoculation by clinically recovered eyes is related to the persistence of active, but subclinical, tuberculous disease. In other words, the idea formerly entertained that an attack of ocular tuberculosis might endow the eye with a local tissue immunity was a chimera. The immunity which existed was transitory and was a cellular phenomenon, dependent probably on the premobilization of macrophagic cells. It is possbile there may have been the additional factor of help from the circulating antibodies, present in the eye in greater concentration as a result of the increased vascularity, but there is no actual evidence on this point. These experiments, therefore, throw no additional light on the nature of immunity, but do confirm the generally held view that in its essence immunity is due to a cellular and humoral reaction.

Barren as this study is of any substantial advance in knowledge, the experimental data recorded give food for thought on the general question of ocular tuberculosis. Comment has already been made on the similarity of experimental ocular tuberculosis in the rabbit to the tuberculous ocular lesions in man with respect to the clinical picture and course of the disease. The demonstration that in experimental ocular tuberculosis subclinical tuberculous lesions smolder in the eye well after the time that all clinical evidence of activity has disappeared is of considerable interest. Also of significance is the observation that in the desensitized group of rabbits reported on in study VII, when tuberculin therapy was stopped, the sensitivity recurred in 4 of 11 eyes which had clinically inactive disease, and the eyes again became acutely inflamed and ruptured.

In the experimental disease the general picture of recovery, with subsequent healing or relapse, appears to be somewhat as follows: As the local tissue sensitivity subsides, either as a result of tuberculin therapy or incidental to a fortuitous decrease in the severity of the disease, the acute inflammatory phase of the process subsides, and the clinical evidences of active inflammation disappear. A phase in which there is apparent recovery, with low tissue sensitivity, follows, but there is still a smoldering and restrained subclinical tuberculosis, with cellular infiltration of the affected tissues. During this phase any new bacilli arriving in the eye find here a low sensitivity and produce little inflammatory reaction. The bacilli are probably promptly phagocytosed by the premobilized macrophages and epithelioid cells. Thus, the eyes for a time appear relatively immune. Thereafter the ocular disease may follow one of two courses, the direction being dependent on such imponderables as the general resistance of the animal and the individual tendency toward hypersensitivity. On the one hand, the subclinical lesions may gradually become encapsulated, the cellular infiltration diminish and disappear and the eyes actually heal, with variable amounts of scarring. In some eyes viable bacilli may still be present, and the essence of the healing in such eyes is probably bacteriostasis, and not complete destruction of the organisms. If the immunity should fade in such animals, the viable bacilli may multiply, with recurrence of the ocular inflammation. In other animals, in which good immunity does not develop, the bacilli in the subclinical lesions may gradually multiply, the tissue sensitivity recur and, with return of the local sensitivity, a relapse of the disease occurs with acute inflammation, necrosis and caseation. There is apparently no such thing as local tissue immunity.

If this concept of the process is applied to ocular tuberculosis in man, there are obvious lessons to be learned. The apparent healing of a tuberculous lesion, with subsidence of clinical evidences of activity, should not be regarded with too much complacency or undue satisfaction. It must be realized that the eye has passed only into the first phase of the actual healing process, however elated both the patient and the physician may be with the apparent recovery. Efforts should be continued to promote the general health and resistance of the patient and to prevent the recurrence of tissue hypersensitivity. The significant experimental observation on this point is the fact that within one year after cessation of tuberculin therapy, sensitivity recurred, the immunity declined and the bacteria began to grow in 4 of 11 desensitized and apparently

healed rabbit eyes, and that with this return of sensitivity there was renewed ocular inflammation, with caseation and necrosis. It is quite possible that, with further passing of time, the same process might have occurred in other rabbits of this group. Such an experimental result, if applied to clinical ophthalmology, is a definite indication that tuberculin should be continued for a long period in order that relative tissue insensitivity may be maintained. Unfortunately, the phenomenon of immunity is far from being completely understood.

SUMMARY

An experimental study of the increased resistance manifested by the eyes of rabbits which had recently recovered from an attack of ocular tuberculosis revealed that this increased resistance was transitory, gradually diminishing after four months and completely absent after one year. It was not related to enhancement of the general immunity, to a decrease in the reaction capacity of the eyes or to the increase in vascularization resulting from the former infection.

It was found that eyes which had every clinical evidence of subsidence of all active inflammation still showed smoldering tuberculous foci and cellular infiltration when examined microscopically. As these eyes completely recovered and these microscopic evidences of activity faded, the resistance to reinoculation likewise disappeared.

A study of the status of the ocular sensitivity of rabbits which had been almost completely desensitized one year before, and for which tuberculin therapy had been discontinued for one year showed a return of the sensitivity and a recurrence of the ocular tuberculosis in 36 per cent of the animals. On the basis of these experimental results, it is concluded that the resistance to reinoculation in the experimental rabbit with ocular tuberculosis is a transitory and a cellular phenomenon, dependent probably on the premobilization of macrophages.

Wilmer Ophthalmological Institute.

LEPTOTRICHOSIS CONJUNCTIVAE

A FURTHER REPORT

SANFORD R. GIFFORD, M.D.,† AND ALEXANDER A. DAY, M.D.
CHICAGO

In the discussion on a paper by Hurst, one of us (S. R. G.)[1] summarized the cases of leptotrichosis of the conjunctiva in which a thread mold had been observed in sections in our laboratory, and a case was mentioned in which cultures of the organism were obtained. Other cases have been seen since this time, and it seems worth while to review this material.

REVIEW OF LITERATURE

A brief review of the literature will include only the reports of cases in which the leptothrix, or a thread mold presumed to be the leptothrix, was seen in sections or culture. A discussion of the oculoglandular syndrome of Parinaud has been published elsewhere by Gifford and Dillon,[2] and most American ophthalmologists are familiar with the three diseases which may be grouped under this name: tuberculosis of the conjunctiva, the oculoglandular form of tularemia and leptotrichosis conjunctivae.

The observation of the leptothrix in sections of material from cases of a condition known as Parinaud's conjunctivitis was first made by Verhoeff,[3] in 1913. A special staining technic was necessary to demonstrate the organism, and it was found only when a characteristic area of focal necrosis was excised and the tissue fixed in Zenker's fluid. In his latest report Verhoeff[4] reported having observed the organism in specimens from 54 of 56 cases in which the tissue showed the characteristic histologic picture described by him. He advised the staining of a number of sections with hematoxylin and eosin and selection of one or two sections presenting the characteristic picture of phagocytosis of necrotic material by microphages; these sections are then stained by his modified Gram method without decolorization of the hematoxylin and eosin stain. It is only in this way, he stated, that areas containing the threads may be detected. In material not showing this picture the threads are not seen, and this was true of material from a number of cases submitted to him which were not included in his series. In many instances the material had been submitted to him by other ophthalmologists, and such cases, with Verhoeff's observations, were reported by Keiper,[5] Lemoine[6] and Dunphy.[7]

In 1927, one of us (S. R. G.)[8] reported identification of the organisms in 2 cases, in 1 of which a single large granulation was excised. This was presumed to be the primary lesion, since a foreign body, probably of vegetable origin, was observed embedded in the tissue and surrounded by organisms. Excision was followed by the appearance of other typical areas of focal necrosis, and the condition ran a characteristic course. These 2 cases were the first in which the organism had been seen outside of Verhoeff's laboratory. In 1934 a third case in which the organism was identified was reported by Gifford and Dillon.[2] In 1936 Lamb[9] observed leptothrix filaments in sections from 2 typical cases.

Hurst,[10] in a series of 23 cases of oculoglandular disease, reported the observation of leptotriches in sections from 4 cases. In 2 of these 4 cases, to be referred to later, the identification was made in our laboratory, the observations in the others being made by Dr. Harvey Lamb, of St. Louis, and by Dr. Verhoeff. In this series of cases of oculoglandular disease were 2 instances of oculoglandular tularemia in which agglutination tests gave positive results and 17 cases in which no agent could be seen, although in only 3 of these was tissue removed for study.

† Dr. Gifford died on Feb. 25, 1944.

From the Departments of Ophthalmology and Bacteriology, Northwestern University Medical School.

1. Gifford, S. R., in discussion on Hurst.[10]
2. Gifford, S. R., and Dillon, E. E.: Conjunctivoglandular Syndrome of Parinaud: Report of Case Showing Thread Mold in Sections, Arch. Ophth. **12:** 518 (Oct.) 1934.
3. Verhoeff, F. H.: Arch. Ophth. **42**:345, 1913; **63**:345, 1918; Am. J. Ophth. **1**:702, 1918.
4. Verhoeff, F. H.: Leptotrichosis Conjunctivae (Parinaud's Conjunctivitis) Without Glandular Involvement: Report of Case, Arch. Ophth. **25**:1 (Jan.) 1941.
5. Keiper, G. F.: Ann. Ophth. **22**:780, 1913.
6. Lemoine, A. N.: Parinaud's Conjunctivitis with Demonstration of Leptothrix of Verhoeff, J. A. M. A. **82**:537 (Feb. 16) 1924.
7. Dunphy, E. B.: Am. J. Ophth. **9**:669, 1926.
8. Gifford, S. R.: Am. J. Ophth. **10**:484, 1927.
9. Lamb, H. D.: Am. J. Ophth. **19**:571, 1936.
10. Hurst, V. R.: Am. J. Ophth. **22**:891, 1939.

Early attempts to cultivate the organism were usually unsuccessful. Wherry and Ray[11] cultured material from the preauricular gland of a patient and isolated an unbranched thread mold which, although it was gram-negative, they claimed to be identical with the leptothrix described by Verhoeff. Growth was on Dorset's egg medium under anaerobic conditions. In 1933 Verhoeff and King[12] obtained cultures of the leptothrix in 3 out of 4 cases. They employed excised conjunctival tissue, and growth was positive only on serum agar and dextrose agar under 10 per cent carbon dioxide tension. Sections of tissue in all these cases showed the organism, and subconjunctival injections of organisms grown in culture produced lesions in rabbits. In a later report[4] Verhoeff stated that culture of material from 7 subsequent cases resulted in growth in only 2 cases, though in all but 1 of these cases organisms were present in sections. Verhoeff employed excised tissue for culture and did not aspirate material from the glands. It is noteworthy that in 1 of his cases in which numerous organisms were noted in sections no preauricular adenopathy was present, this being the only case of the kind on record. Culture of material did not yield the organism in this case, and Verhoeff recommended examination of tissue as much more reliable than culture in diagnosis.

In 1937 Wright[13] cultivated leptotriches from fluid aspirated from the preauricular gland in a case. Primary cultures were grown under anaerobic conditions on Soparkar's heated human blood medium at 30 C., hydrocele agar and ordinary agar enriched with a surface smear of human blood. Subcultures were obtained under both aerobic and anaerobic conditions. Wright expressed the belief that culture should be simpler and more reliable for diagnosis than the study of sections. He described the identification of the organisms by Verhoeff's method in sections from typical cases of the disease, but he did not report these cases. The organism isolated by Wright was gram-positive, while that cultured by Wherry and Ray and at least two strains grown by Verhoeff and King were described as gram-negative. In sections the granules in the threads and some of the threads were gram-positive, while parts of the threads are decolorized.

Since the report of Gifford and Dillon, in 1934, material from 14 cases has been examined in our laboratory. Most of the patients were seen personally by one of us (S. R. G.), some having been referred by other ophthalmologists for excision of the material. In all but 2 cases the typical clinical picture described by Verhoeff was noted. Of the exceptions, 1 was a case of oculoglandular tularemia in which positive agglutination reactions were later obtained, and in the other no definite areas of focal necrosis, but only large follicles in the upper fold with adenopathy, were observed. Material alone was examined from 7 cases, submitted by Dr. V. R. Hurst, of Longview, Texas; Dr. W. H. Morrison, of Omaha; Dr. Harold Gifford, of Omaha; Dr. W. M. Scales, of Hutchinson, Kan., and Dr. W. H. Theobald, of Chicago. It is assumed from the histories submitted, and in 1 case from a kodachrome photograph, that all these 7 cases showed the typical clinical picture of Parinaud's oculoglandular syndrome. Hence, except for the 2 cases aforementioned, material was available from 12 cases in which leptotrichosis conjunctivae was, with good reason, suspected.

Without any detailed discussion of the histopathologic changes, it may be said that the specimens in all 12 cases showed the histologic picture described by Verhoeff. In 8 of these cases Verhoeff's modified Gram method revealed granules and threads of a thread mold, presumably leptothrix, in sections, while in 4 cases no such elements could be seen. The 8 cases in which the organism could be identified and the 3 cases already reported make a total of 11 cases in which leptothrix has been identified in sections by one of us (S.R.G.). The organisms were approximately of the same size in all cases, but their distribution in the tissues varied considerably (figure). In several specimens dilated capillaries were filled with granules and threads, an observation not reported by Verhoeff. In other specimens large mononuclear cells contained masses of gram-positive granules, among which short chains of granules could be made out by careful focusing. It requires some familiarity with the appearance of the leptothrix in sections for one to be sure of identification in certain specimens, and it is particularly difficult to photograph the organisms. This, in addition to the necessity of obtaining the essential lesions in the specimen and of a careful staining technic of material fixed in Zenker's fluid, probably accounts for the negative reports in a number of cases.

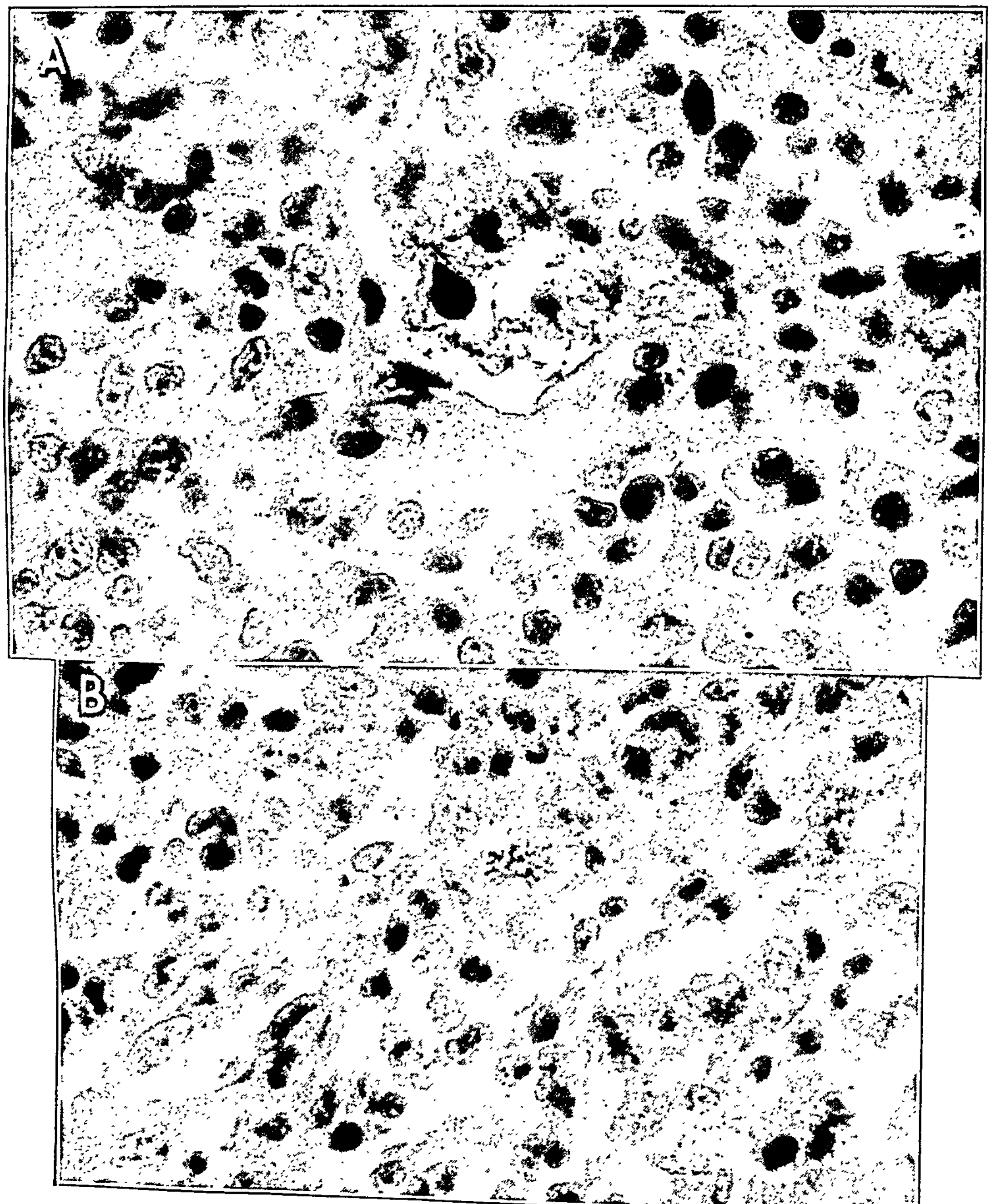
Material was cultured in 3 cases according to the technic described by Verhoeff and King, with the addition of Soparkar's medium, as advised by Wright. In all 3 instances material for culture

11. Wherry, W. B., and Ray, V.: J. Infect. Dis. **22**:554, 1918.

12. Verhoeff, F. H., and King, M. J.: Leptotrichosis Conjunctivae (Parinaud's Conjunctivitis): Artificial Cultivation of Leptotriches in Three or Four Cases, Arch. Ophth. **9**:701 (May) 1933.

13. Wright, R. E.: Isolation of Verhoeff's Leptothrix in Case of Parinaud's Syndrome, Arch. Ophth. **18**:233 (Aug.) 1937.

was obtained by aspiration from a swollen preauricular gland, while in 1 of these cases material excised from the upper fornix was used as well. In only 1 of these cases was the leptothrix grown in culture, the results of culture in 1 of the others being negative and a growth of saprophytes of no significance being obtained in the other. In all these 3 cases leptothrix elements appeared in sections of the conjunctival lesion, and in 1 of the cases in which cultures of material from the with the cultures grown under anaerobic conditions, the cultures kept at 10 per cent carbon dioxide tension being negative for the organism. The colonies developed only after seven days' incubation. Subcultures grew aerobically on the usual mediums. Gelatin and blood serum were liquefied, but no fermentation of dextrose, lactose, sucrose or maltose occurred. No hemolysis was produced. Milk cultures became alkaline. The organisms grown in culture were long



Photomicrographs, showing (*A*) leptothrix threads in an enlarged capillary and (*B*) granules and short threads in an epithelioid cell.

gland were negative, so many leptothrix elements were noted in the conjunctival lesions as to make it seem likely that they would have grown in culture if material from such a lesion had been used for this purpose.

Briefly, the characteristics of the leptothrix isolated from a single case were as follows:

The material was a few drops of cloudy fluid aspirated from a swollen preauricular gland. Original inoculation was on human blood agar slender rods and threads, which formed terminal spores after seventy-two hours. They were uniformly gram-negative. This was true of the organisms isolated by Verhoeff and King, although in sections the organisms were gram-positive with Verhoeff's stain, as were ours. It was easy to decolorize them with oil of organum, however, and there seems to be no doubt that the organism obtained in culture was the same as that seen in sections. It may be mentioned

that the strains of leptothrix isolated by one of us (S. R. G.) from a case of a different type of chronic conjunctivitis and from a case of meibomitis were gram-postive in smears and cultures.

Subconjunctival injection of the organism in a sphinx baboon gave no reaction in forty-eight hours. Similar inoculation in a rabbit produced a profuse discharge from and swelling of the conjunctiva. The rabbit died after three days, and the organism was recovered from the conjunctiva in mixed culture. Death was apparently due to an intercurrent infection, as other organisms were grown from the viscera and heart's blood.

These results make us inclined to agree with Verhoeff that the examination of properly fixed and stained material in sections offers a greater likelihood of obtaining positive identification of the leptothrix than the use of cultures. The value of cultures in addition to sections, however, should not be minimized, as exact identification of the organism in a greater number of cases is certainly desirable.

The accompanying table will perhaps serve to review the salient features of the group of diseases which may be classified under the general name "conjunctivoglandular syndrome of Parinaud" and will give an idea of the relative frequency of the diseases in the districts surrounding Omaha and Chicago. Under leptotrichosis conjunctivae are classified only cases from the present and former reports in which positive identification of the threads was made in sections by one of us (S. R. G.), and under the syndrome "of unknown origin," cases in which sections were made but no organisms were seen. A few cases in which no material was removed are not included.

Data on Cases of the Conjunctivoglandular Syndrome of Parinaud

	No. of Cases	Local Signs	Blood Picture	Febrile and Systemic Reactions	Positive Laboratory Findings
Oculoglandular tularemia.......	1	Focal necrosis and ulcers	Leukocytosis	Usually severe	Agglutination of Pasteurella tularensis after 2d week
Tuberculosis of the conjunctiva	1	Usually one ulcer	No change	Usually absent	Acid-fast bacilli in scrapings; positive guinea pig inoculation
Leptotrichosis conjunctivae.....	15	Small areas of focal necrosis; granulation	Eosinophilia, count of 3 to 10% in 50% of cases	Moderate in first week	Elements of thread mold in sections of lesion stained by Verhoeff's method; characteristic histopathologic picture; cultures may be positive for the leptothrix
Conditions of unknown origin .	7	Variable; usually same as in leptotrichosis	Variable	Moderate in first week	None; sections may show histopathologic picture resembling that of leptotrichosis *

* This picture was not noted in Verhoeff's material.

It is evident that, at least in the Middle West, leptotrichosis conjunctivae is much more common than either conjunctival tuberculosis or oculoglandular tularemia. It is probable that with more exact clinical observation and the use of available laboratory methods in every case in which this syndrome is present, the number of cases of the disease classified as "of unknown origin" would be reduced to an even smaller figure than that shown in the table. In every case agglutination tests with Pasteurella tularensis should be employed, and, if the reactions are negative, a piece of tissue containing a characteristic lesion should be fixed in Zenker's fluid and submitted to adequate examination.

Northwestern University Medical School.

FUNDUS OCULI IN UROLOGIC DISEASES ASSOCIATED WITH SYSTEMIC HYPERTENSION

MARTIN COHEN, M.D.
NEW YORK

This paper will be limited to the consideration of three urologic diseases associated with hypertension: pyelonephritis, hydronephrosis and polycystic kidney. These diseases may exist independently, or they may be combined. In several patients with one or another of these conditions, who were referred to me during the past year for an ophthalmologic report, examination disclosed various grades of lesions of the fundus.

In reviewing the ophthalmologic literature, I was unable to find any paper on this subject, although Longcope,[1] Weiss and Parker[2] and other internists and urologists in their papers on pyelonephritis and other urologic conditions reported the presence of lesions of the fundus. It is significant to find that in severe urologic diseases with persistent hypertension the changes in the fundus are similar to those observed with essential hypertension, chronic glomerulonephritis, toxemia of pregnancy and, rarely, arteriosclerosis. The question whether the hypertension or the urologic disease or both are responsible for the lesions in the fundus is still an open one. Some urologists and internists have stated that, from their clinical examinations, they believe that the hypertension is secondary to the urologic disease. Accordingly, another question to be considered is whether the high blood pressure existed in these patients as an independent condition (essential hypertension) or whether it was the result of the urologic disease (secondary hypertension). I do not consider urologic disease associated with persistent high blood pressure and lesions in the fundus a clinical entity, but still it is a frequent combination. Any pathologic condition of the kidney, affecting to any extent its blood supply or its urinary drainage, may, if not relieved, cause vascular structural changes, with such a resulting disturbance as renal ischemia. Some authorities consider the renal condition to be the basic cause of hypertension. The hypertension results in arteriolar spasm, sclerosis and other lesions affecting the vital organs, including the fundus oculi. The lesions in the fundus may be progressive or retrogressive. The prognosis of the urologic disease with hypertension rests chiefly on the condition of the vital organs. The signs in the fundus are often the visible guide to the condition of the cardiovascular-renal system.

CLINICAL CONSIDERATIONS

I shall consider briefly some clinical facts pertaining to the urologic diseases mentioned. These diseases are due either to an ascending or descending acute or chronic infection of the urinary passages or to a urinary obstruction, caused by such agents as calculus, stricture, an enlarged prostate or congenital anomalies. A physical examination is obviously required, as well as a report on both kidneys. Examination should include roentgenographic, pyelographic and cystoscopic studies, as well as tests for renal function, examination of urinary smears, determination of the blood pressure and examination of the fundi.

Pyelonephritis.[3]—This disease is an infection of the pelvis and parenchyma of the kidney, which is frequent, especially in children, and is often due to the colon bacillus. It may progress from an acute to a chronic stage and may result in a pyelonephritic, atrophic kidney with extreme hypertension.

CASE 1.—R. S., a man aged 43, a truckman, was admitted to the clinic on March 5, 1943. His physician reported that he had had persistent high blood pressure for the last fourteen months. He was married and had 2 healthy children. He had never suffered previously from any serious disease, but he gave a history of nocturia and transient amblyopia. He complained chiefly of attacks of severe occipital headache, lasting two hours. He had had an attack of Bell's palsy two weeks before admission to the clinic. Medical treatment was of no avail. He was referred to me for an examination of

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From the Department of Ophthalmology, in cooperation with the Departments of Medicine and Urology, of the New York Post-Graduate School and Hospital.

1. Longcope, W. T.: Chronic Bilateral Pyelonephritis: Its Origin and Association with Hypertension, Ann. Int. Med. **11**:149-163 (July) 1937.
2. Weiss, S., and Parker, F., Jr.: Pyelonephritis: Its Relation to Vascular Lesions and to Arterial Hypertension, Medicine **18**:221-315 (Sept.) 1939.
3. Barker, N. W., and Walters, W.: Hypertension Associated with Unilateral Chronic Atrophic Pyelonephritis: Treatment by Nephrectomy, Proc. Staff Meet., Mayo Clin. **13**:118-121 (Feb. 23) 1938.

the fundus, which resulted in a diagnosis of bilateral neuroretinopathy associated with pyelonephritis.

On April 1 he was transferred to the medical ward of the hospital. An abstract of the hospital record shows that the blood pressure ranged from 200 systolic and 140 diastolic to 180 systolic and 110 diastolic. The renal function was normal. The urine showed mild proteinuria but was otherwise normal, with no colon bacilli or pus cells. Intravenous urographic and retrograde pyelographic examinations revealed a normal condition of the left kidney and lobulation of the right kidney, with uncertain filling of the renal pelvis. These findings suggested the presence of a neoplasm; therefore it was decided, after consultation, to remove the right kidney. The patient's blood pressure was not lowered after the operation, but the headaches were relieved. On May 5 he was discharged from the hospital and was advised to return to the clinic. Microscopic examination of the removed kidney (fig. 2) revealed a wedge-shaped area of scarred tissue, extending to the pelvis of the kidney, as well as sclerosed and narrowed blood vessels. Large foci of mononuclear cells surrounded the vessels. Many glomeruli were hemorrhagic, and others were partly sclerosed. The diagnosis was pyelonephritis of the right kidney and anterior malposition of its pelvis.

Examination of the Fundus: The results of examination a week after nephrectomy were as follows (fig. 1): The lesions were similar to those seen before the operation; they were practically identical in the two eyes. The optic disk and the surrounding area were edematous; the macular area was normal. The retinal veins were uniformly congested; they were also compressed and deflected where they were crossed by hyalinized arterioles. The arterioles were narrowed; some were of irregular caliber; others showed a prominent central light reflex. Located near the macular area were numerous glistening, sharply defined, whitish foci, the result of lipid degeneration. Similar foci of lipid material were also present above and nasal to the disk. A large whitish retinal plaque was located in the vertical meridian, at some distance below the disk. This was caused by a lymphocytic exudate and was surrounded by hemorrhages. Flame-shaped hemorrhages were visible above and below the disk. The diagnosis based on the appearance of the fundus was bilateral neuroretinopathy accompanying pyelonephritis, with hypertension.

Subsequent Course: A recent ocular examination at the clinic, on September 23, revealed the following status: Vision remained 20/30 in each eye, as noted prior to the operation. Neuroretinal edema was now increased. The blood pressure was 230 systolic and 130 diastolic; the excruciating headaches had returned; renal function was normal, and proteinuria was present.

The case came up for discussion at a medical conference at the hospital on September 23. The general impression was that the pyelonephritis preceded the hypertension and the lesion in the fundus. The patient was readmitted to the hospital on October 10 because of continuous severe headaches and persistent high blood pressure. On October 23 the blood pressure was 216 systolic and 102 diastolic; the urea nitrogen was 46 mg. and the creatinine 4 mg. per hundred cubic centimeters, values indicative of renal involvement. Vision was the same as that previously noted. Additional changes had developed in the fundus: Papilledema of 3 D., as well as profuse fresh retinal hemorrhages with exudates, was present in the right eye; changes in the left eye were similar except that the elevation of the disk measured 2 D.

On October 30, because of the persistent excruciating headaches, a bilateral splanchnic sympathectomy (Smithwick[4]) was performed. A week later the elevation of the disks had subsided, while the retinal changes remained the same. The blood pressure was 172 systolic and 108 diastolic; the urea nitrogen measured 33 mg. and the creatinine 3.2 mg. per hundred cubic centimeters, a decrease indicating reduction in the hypertension and improvement in renal function.

In a review of this case, it is evident that the nephrectomy and the absolute rest of seven months had no beneficial effect on the secondary hypertension. The increased lesions in the fundus and the impairment of renal function indicated progression of the underlying disease. The sympathectomy improved the renal function and reduced the hypertension, as well as the edema of the disk. It is obviously too soon after the sympathectomy for any prognosis with regard to the outcome in the case.

I noted a similar case of unilateral pyelonephritis with nephrectomy in a paper published earlier this year.[5]

Hydronephrosis.[6]—CASE 2.—M. R., a man aged 43, a merchant, was married and had 2 healthy children Physical examination showed a normal condition except for pain over the lower part of the spine and foul, bloody urine. The patient first consulted a physician in 1931 and had been examined at intervals since. In 1935 an excretory urogram showed nothing abnormal. Cystoscopic examination showed a tumor at the neck of the bladder, and a suprapubic excision was performed. The microscopic diagnosis of the growth was carcinoma, and radium seeds were planted in the bladder. After a few weeks pyelonephritis developed on the right side, as a result of infection of the bladder, and nephrectomy was required. In February 1937 the patient reentered the hospital for a check-up. Pyelograms taken at this time revealed bilateral hydronephrosis. A cystoscopic examination disclosed no recurrence of the carcinoma. He was discharged and advised to report to his physician at regular intervals.

On Jan. 14, 1943 I examined the patient for the first time, because of sudden blurring of vision. Vision was 20/30 in the right eye and 3/200 in the left eye. Functional tests, including measurement of intraocular tension, gave normal results. His blood pressure was 260 systolic and 140 diastolic, and there were pronounced lesions of the fundus. He then consulted his physician, who referred him to the hospital, on Jan. 18, 1943, for reexamination and treatment. Studies then showed poor excretory function in both kidneys and moderate increase in the urea content of the blood (25.3 mg. per hundred cubic centimeters), associated with diminution of vision and pronounced hypertension. The patient was discharged four days later. The urologic diagnosis was bilateral hydronephrosis with hypertension.

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4. Smithwick, R. H.: A Technique for Splanchnic Resection for Hypertension, Surgery **1**:1-8 (Jan.) 1940.

5. Cohen, M.: Fundus Oculi in Hypertensive Vascular Diseases, Arch. Ophth. **29**:85-91 (Jan.) 1943.

6. Keith, N. M., and Pulford, D. S., Jr.: Experimental Hydronephrosis: Functional Anatomic Changes in the Kidney Following Partial Ureteral Obstruction, Arch. Int. Med. **20**:853-878 (Dec.) 1917.

Examination of the Fundus: The changes in the fundus were as follows (fig. 3): In the right eye, the optic disk was hyperemic and its margin blurred. The disk was completely surrounded by a large whitish patch, which was mottled, with threadlike, brownish markings, and had a sharply indented margin. Retinal vessels crossed the patch. These changes may indicate a preexisting extensive exudate, which, on being resorbed, left the diffuse whitish scar. The macular area was made up of glistening lipid dots surrounded by pigment. Lipid foci were also seen in the periphery of the fundus. The retinal veins were tortuous and bordered by white lines, a condition indicating periphlebitis. The arterioles were mostly obscured; a single arteriole was visible below the disk. There was a small circular hemorrhage in the whitish patch. The diagnosis based on the appearance of the fundus was neuroretinopathy, with a large peripapillar exudate associated with hydronephrosis. In the left eye, the disk was edematous, and the macular area showed chorioretinal foci of degeneration. The retinal veins were moderately engorged; they were tortuous, and some were compressed by sclerosed arterioles. Many arterioles were obscured, and those which were evident were narrowed. The central light reflex in some vessels was prominent. An isolated retinal hemorrhage was located above the disk. The diagnosis based on the appearance of the fundus was neuroretinopathy associated with hydronephrosis, with hypertension.

Subsequent Course: On October 11 I reexamined the patient. He now complained of deterioration of his general health. Inspection of the fundi showed an increase in the retinal lesions, and the blood pressure was also elevated.

Since the patient had been free from hypertension before the onset of most of the urologic symptoms, it may be assumed that the hypertension followed the renal involvement and that the urologic treatment produced no beneficial results. This was evident from the sustained high blood pressure and the increase in the lesions of the fundus, which suggested a grave prognosis.

Polycystic Kidney.[7]—CASE 3.—N. L., a man aged 34, a salesman, was married and had 1 healthy child. He appeared well nourished and had never suffered from any serious disease before the present hematuria. He stated that his father and a brother died of polycystic kidney. In 1928, in the course of his being examined for insurance, proteinuria and hypertension were discovered. Roentgenographic and cystoscopic examinations at that time revealed nothing significant. He had been admitted to the hospital on four occasions because of gross hematuria, the first visit being in November 1932. At that time his blood pressure was 176 systolic and 130 diastolic, and study of the eyegrounds showed chorioretinal arteriosclerosis. Urinalysis revealed pronounced proteinuria, but the urea nitrogen content was normal. The second admission was in December 1934, for another attack of hematuria. The blood pressure was then 180 systolic and 130 diastolic; urea nitrogen was 43 mg. and creatinine 3.2 mg. per hundred cubic centimeters. He had normal vision.

Examination of the Fundi (fig. 4): The disk was pale, due to sclerosis of the capillaries on the disk. The margin was sharply outlined. The macular area was normal, as were the retinal veins. The arterioles were narrowed. There was a small circular retinal hemorrhage in the periphery of the right fundus. In the outer zone there was an area of retinal depigmentation, which allowed visualization of the choroidal stroma. This area was possibly the result of localized sclerosis of the choriocapillaris. The appearance of the fundus was practically the same in the two eyes. The diagnosis based on the condition of the fundus was bilateral chorioretinal arteriosclerosis, with hypertension.

The third admission occurred in January 1936, after an attack of gross hematuria, with a blood pressure of 184 systolic and 128 diastolic. In June 1936, after another attack of hematuria, preceded by a chill and abdominal pain, the patient was admitted to the hospital for the fourth time. The blood pressure was 172 systolic and 110 diastolic. An intravenous urogram revealed notable enlargement of both kidneys. A retrograde pyelogram showed the typical bilateral renal changes of polycystic disease, with marked dilatation of both the pelvis and the calices. There were profound anemia and definite proteinuria, with innumerable red blood cells. Urea nitrogen was 76.1 mg. per hundred cubic centimeters. An abdominal examination disclosed a palpable mass in the left costal area, and resistance, suggestive of a mass, was also felt on the right side. The diagnosis was polycystic renal disease and azotemia. In 1937, after another attack of hematuria, the patient was admitted to another hospital. According to the records there, his blood pressure at that time was 172 systolic and 128 diastolic. The urea of the blood was 197 mg. per hundred cubic centimeters. Examination of the fundus showed only a small circular retinal hemorrhage in the right fundus. The patient died of retention uremia, five days after admission.

In this case it is significant that the continuous high blood pressure and the disturbance of renal function for at least four years caused no neuroretinopathy in either fundus but simply bilateral chorioretinal arteriolosclerosis. The diagnosis of chronic glomerulonephritis was considered in this case, but, because of the absence of neuroretinopathy for so long a period, with hypertension and azotemia, I believe that this diagnosis was untenable, except in its terminal stage.

SUMMARY

The purpose of this paper is to call to the attention of ophthalmologists the lesions in the fundus associated with urologic diseases. Some internists and urologists have reported the presence of such lesions in connection with these conditions.

Bilateral neuroretinopathy, possibly of inflammatory origin, was the condition in the case of pyelonephritis and that of hydronephrosis reported here, while in the case of polycystic kidney the diagnosis was bilateral chorioretinal arteriolosclerosis of noninflammatory origin.

Further investigation is necessary to ascertain whether inflammatory or noninflammatory lesions

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7. Schacht, F. W.: Hypertension in Cases of Congenital Polycystic Kidney, Arch. Int. Med. **47**:500-509 (March) 1931.

occurring with urologic disease produce corresponding lesions of the fundus.

It can be stated that urologic diseases, accompanied by persistent high blood pressure, usually lead to lesions of the fundus.

The changes in the fundus, as revealed by the detailed study of these cases, are indicative of the severity of the underlying hypertensive vascular disease, regardless of the factor or factors responsible for the elevation of the arterial tension.

A report on the examination of the fundus should accompany the records of cases of urologic diseases with persistent hypertension, as it is an additional aid to the diagnosis and prognosis of the disease.

29 East Sixty-Fourth Street.

DISCUSSION

Dr. Arthur M. Fishberg, New York: The presence of hypertensive neuroretinopathy in a case of undoubted primary renal disease proves beyond cavil that renal disease itself can cause lesions of the fundus. However, all the evidence indicates that the only way in which renal disease can cause these lesions is through the mediation of high blood pressure; there are no changes in the fundus. The incidence of retinal lesions in any renal disease strictly parallels the elevation of the blood pressure; moreover, it parallels the elevation of the diastolic, and not the systolic, pressure. Even with the most pronounced elevation of systolic pressure there will be no retinal lesions as long as the diastolic pressure is not elevated. The best evidence of this is derived not from cases of renal disease but from those of aortic regurgitation in young people who run high systolic pressures, even close to 300 mm. of mercury, for years without a rise in diastolic pressure, and never have lesions of the fundus. The evidence is clear; the parallelism is with the diastolic pressure. Any measure that reduces the diastolic pressure is likely to result in clearing up of the retinal lesions. Good examples are seen in cases of toxemia of pregnancy and in those of successful sympathectomy; when the blood pressure is reduced, the retinal lesions improve or clear up altogether. It may thus be said to be definitely established that the elevation of diastolic pressure in some way produces the retinal lesions, but I cannot state how. Since the days of Volhard it has been conventional to say that it is due to angiospasm in the retina.

For a time it seemed probable that the elevation of intracranial pressure might be connected with lesions of the fundus. Pickering showed that of 23 cases of malignant hypertension, the cerebrospinal fluid pressure was definitely elevated in 22, but I doubt whether this in itself could be the cause of the papilledema and the retinal lesions. The evidence comes from another branch of pathology. Whenever there is elevation of venous pressure, due either to heart failure or to mediastinal compression, there is always a corresponding elevation of cerebrospinal fluid pressure. No matter how high the venous pressure rises, it is always exceeded by the cerebrospinal fluid pressure. Whenever there is such a pure elevation of cerebrospinal fluid pressure, there is never papilledema or other retinal lesion. Friedfeld and I reported on 70 patients with heart disease, none of whom had retinal lesions or papilledema, and in patients with mediastinal tumors we found corresponding elevations of the cerebrospinal fluid pressure, without any changes in the fundus. Internists who attribute the papilledema in cases of malignant hypertension solely to an increase in the cerebrospinal fluid pressure do not have the entire explanation.

Another point that I wish to stress is the importance to the ophthalmologist of the concept of malignant hypertension. Malignant hypertension is not a disease, but a clinical picture that can result in any form of high blood pressure, providing the blood pressure rises high enough for a sufficiently long time. It occurs with glomerulonephritis, with the Cushing syndrome, with pyelonephritis and with other urologic conditions described by Dr. Cohen. In each of these diseases one can differentiate a malignant phase of the hypertension, that is, a malignant phase of essential hypertension, of glomerulonephritis or of pyelonephritis. The ophthalmologist makes his diagnosis on the basis of the clinical picture produced by the increased diastolic pressure. Papilledema and exudates mean that this particular form of hypertension has entered the malignant phase. They indicate that at autopsy rapidly progressive changes in the arterioles—arteriolar necrosis and so-called endarteritis—will be encountered. There is a tendency to the rapid deterioration of renal function, so that a large percentage of patients with this condition die in uremia. The presence of cotton wool exudates and papilledema demonstrates that the disease has entered a phase in which the elevated diastolic pressure is acutely affecting the blood pressure in various organs, including the kidney, where it does its greatest damage.

Dr. Herman Elwyn, New York: I enjoyed the discussion by Dr. Fishberg. In speaking of hypertension, one should always signify the kind meant, whether essential or of renal origin.

The benign phase of essential hypertension has no changes in the fundus. There is no arteriospastic contraction anywhere in the body. The Goldblatt experiment is not represented here. There is nothing but high blood pressure, which may bring on later complications.

Something has been added when essential benign hypertension, which has existed for ten or twenty years, suddenly becomes malignant.

This something is the general arterial contraction in many organs, including the kidneys, the brain and the eyes. This contraction is responsible for the high diastolic pressure and the change from benign hypertension to malignant disease.

Hypertension of renal origin is always secondary to an endangered filtration pressure. The Goldblatt experiment is just that; here a clamp on the renal artery endangers the normal intraglomerular filtration pressure. In consequence, there is a general arterial contraction, and renal hypertension is always the result. Arteriospastic contractions cause changes in the terminal vessel units, with the resulting peristatic and prestatic conditions, followed by the manifestations of retinal changes. It is important to differentiate between essential hypertension in the benign stage and the hypertension which is caused by arteriospastic contraction. It is the latter which produces the retinal changes.

Dr. Arthur M. Fishberg, New York: If the renal arteries are only slightly constricted in the Goldblatt experiment, there result a certain elevation of blood pressure and a perfectly comfortable dog. The animal does not suffer subjectively from a blood pressure of 200 systolic and 120 diastolic, but if the clamp is tightened so that the pressure is sent to very high levels, the dog becomes very uncomfortable, and everything about him reminds one of what is called malignant hypertension in man. The same mechanism which first produces benign hypertension later causes malignant hypertension, and if the investigator releases the clamp, the hypertension returns to the benign stage. There are cases in which the disease in man acts just like that, with the malignant hypertension dependent on the development of a high diastolic pressure.

In a man of 70 the typical picture of malignant hypertension practically never develops because his aorta is sclerotic; the maintenance of a high diastolic pressure requires elasticity of the aorta, which is absent in a person of that age.

In a large number of cases sympathectomy changes malignant hypertension to what one must call benign hypertension for a considerable period, until the effects of the operation wear off.

I can see no reason for saying that a man has acquired a new disease when malignant hypertension develops after five or eight years of high blood pressure; everything indicates that the "malignant hypertension" is merely an aggravation of the disease that has been present for many years.

Clinical Notes

RHINOCANALICULAR ANASTOMOSIS

Richard Waldapfel, M.D., Grand Junction, Colo

The debates on operations on the tear passages appear, for the most part, to be concluded. Each operator has settled down with the method which he likes best and apparently does not find it necessary to add anything new. Yet the procedure which was recently reported by Blumenfeld [1] is so unique and original that it necessitates a brief discussion.

Blumenfeld reported a case in which, after four previous operations on the tear sac, two fistulas formed in the skin, 0.5 cm. medial to the inner canthus. These fistulas represented the distal openings of the upper and lower canaliculi. He excised an oval piece of skin containing the two fistulas. Then, through a window in the bony lateral nasal wall, he exposed the nasal mucous membrane, incised it longitudinally and inserted the oval flap of skin, with the canaliculi attached, into this opening in the nasal mucous membrane. He then joined the edges of the cutaneous flap to the edges of the nasal mucous membrane by stitches, so that a communication of the fistulas with the nasal cavity was established. The primary incision in the skin was then completely closed.

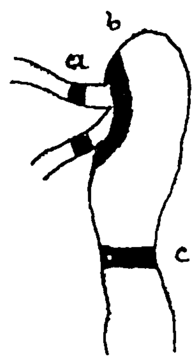

Fig. 1.—Sketch of the tear sac, with both the canaliculi and the first part of the nasolacrimal duct. The black bands represent the different sites of obstruction of the tear passages: (*a*) in the canaliculi; (*b*) in the upper part of the tear sac, near the openings of the canaliculi, and (*c*) in the lower part of the tear sac and the nasolacrimal duct.

It seems to me that this method, if it proves satisfactory in other cases, should have a place in the surgery of the tear passages. It is not suitable, however, in all cases of chronic suppurative dacryocystitis, as Blumenfeld anticipated, but only in certain cases, which can be selected rather simply.

Obstruction in the tear passages may be situated in the following places: in the canaliculi; in the upper part of the lacrimal sac, adjacent to the canaliculi, or in the lower part of the sac and the nasolacrimal duct. These sites are designated as *a, b* and *c* in figure 1. The most frequent occurrence of obstruction in 85 per cent of cases is at *c*. In order to determine the site of obstruction, the canaliculus test is used. When the

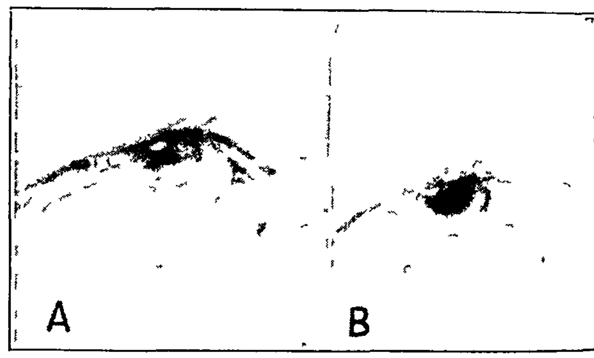

Fig. 2.—L. N., aged 61, with chronic dacryocystitis, epiphora of the right eye and a fistula, 0 5 cm below the inner canthus, of several years' duration. *A*, appearance before the operation Fluid injected into the lower canaliculus passed through the fistula and the upper canaliculus (positive canaliculus test). *B*, appearance three days after intranasal dacryocystorhinostomy. The epiphora was completely gone, and the fistula was closed, without any external operation. The result is permanent, after two years' observation

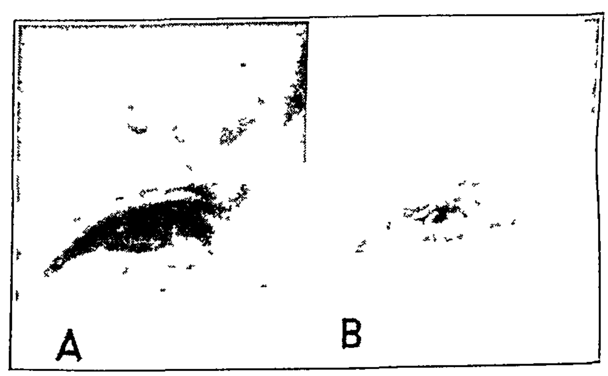

Fig. 3.—C. H. T., aged 70, with chronic dacryocystitis and swelling of the region of the tear sac which frequently was much larger than the picture shows. Epiphora and secretion of pus were present. *A*, before operation, with a positive canaliculus test, and *B*, one day after intranasal dacryocystorhinostomy. The epiphora and swelling were completely gone, without any external operation. The result is permanent, after three years' observation.

1. Blumenfeld, L.: Rhinocanalicular Anastomosis with Reconstruction of the Lacrimal Sac, Arch. Ophth. **31**:248 (March) 1944.

obstruction is at *c*, irrigation of the lower canaliculus will cause the fluid to pass through the upper canaliculus—a positive canaliculus test. When the obstruction is at *a* or *b*, no fluid will pass through the upper canaliculus—a negative canaliculus test. When the canaliculus test is positive, dacryocystorhinostomy is indicated, no matter whether a fistula exists or not. This operation reestablishes normal physiologic conditions by providing for conduction of the tears from the tear sac into the nose, above the stenosis. The fistula closes automatically as soon as the drainage into the nose is instituted without any external operation. Figure 2 shows the appearance of a patient with a fistula before and after the dacryocystorhinostomy. The fistula, which had existed for years, was completetly closed three days after the operation.

The same results are obtained with all swellings in the region of the tear sac in cases of chronic dacryocystitis in which the canaliculus test is positive. The swelling disappears automatically as soon as the drainage in the nose is established, without any external operation. Figure 3 shows such a swelling below the right internal canthus, which had existed for several years and which disappeared immediately and permanently after the dacryocystorhinostomy. In all cases represented by figures 2 and 3, excision of the fistula or the sac is unnecessary. In such cases the dacryocystorhinostomy is, and remains, the method of choice.

Blumenfeld's objections to this operation (West; Toti; Mosher; Halle) are not justified. The statistics for this operation are based on thousands of cases, and the results are analogous to those in the 2 cases illustrated here, successful and satisfactory, with no postoperative manipulations required. The operation offers a cure in almost 100 per cent of cases—if it is properly performed and the cases are carefully chosen, i. e., only those in which the obstruction is at *c*.

The conditions in cases with obstructions at *a* and *b* are different, however. There the dacryocystorhinostomy is not indicated, and other procedures, including extirpation of the tear sac, are often unsatisfactory. It is in such cases, with a negative canaliculus test, in which I see the important field for the new method, a procedure which may fill a gap in the surgical treatment of the lacrimal system.

I think that this clarification is necessary in the interest of the existing valuable methods of operation, as well as in that of the cleverly designed new procedure, in order that it may be accorded the place it deserves.

De Merschman Gardens.

ABSTRACTS OF ARTICLES PUBLISHED IN THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION UNDER THE AUSPICES OF THE SECTION ON OPHTHALMOLOGY, 1943

W. ZENTMAYER, M.D.
PHILADELPHIA

Eye Manifestations of Head Injuries. D. J. Lyle, M.D., Cincinnati, J. A. M. A. **123:** 873 (Dec. 4) 1943.

The subject of ocular manifestations of head injuries is discussed under the headings: concussion, contusion of the brain, laceration, compression and hemorrhage.

The text is illustrated by several case histories.

Most of these injuries fall into three classes: (1) automobile and other travel accidents, which are increasing; (2) industrial accidents, which are multiplied by the acceleration of production to meet the war demands, and (3) head injuries of the war itself.

DISCUSSION

Dr. A. D. Ruedemann, Cleveland: There is a large variety of head injuries. The earliest is that of compression occurring at birth. With the use of forceps, pressure is a factor in the production of hemorrhages at the base of the skull and accounts for a number of cases of squint. Industrial injuries and accidents often involve the head. Severe intermittent headache subsequent to head injury is an excellent diagnostic symptom when most ocular signs disappear. The force of the blow on the orbit may produce a compression fracture in the canal, which can be revealed by the planograph method of roentgenography. Pulsating exophthalmos results from fracture of the base which produces a tear of the internal carotid artery and the cavernous sinus.

Gunshot wounds in the occipital region may give bizarre changes in the visual fields without alterations in the fundus.

Dr. C. W. Rutherford, Indianapolis: War wounds are of greater value to research than those encountered in civilian experience because many more of them are available at one time and they can be studied in groups of cases by specially trained investigators. The studies of Holmes and Lister may be mentioned in this connection (*Brain* 39: 34, 1918).

Dr. W. I. Lillie, Philadelphia: The importance of pupillary changes should be emphasized, as Dr. Lyle did. Patients with fracture of the skull usually have normal ocular signs during their stay in the hospital but may show ocular damage later. The syndrome of traumatic intracranial changes is not unlike that produced by vascular, inflammatory and neoplastic lesions, although the localizing signs may be masked in the earlier stages of convalescence.

Intraocular Foreign Bodies. E. Stieren, M.D., Pittsburgh, J. A. M. A. **123:** 880 (Dec. 4) 1943.

Every patient with an ocular injury of the globe or the soft parts of the orbit should be given an immunizing dose of 1,500 units of tetanus antitoxin, both for its specific effect and for its action as a foreign protein.

When the foreign body lies in the lens, the latter should be removed at the same time by thorough washing of the anterior chamber. If the wound of entrance involves the ciliary body, the eye is to be enucleated immediately. A metallic foreign body is removed through the cornea when it is anterior to the posterior capsule of the lens, and through a scleral incision when it is in the vitreous, in the choroid or on the optic disk. A hand magnet is always used, with only the cone-shaped or the olive-shaped tip.

The magnet should never be used as a diagnostic instrument. A live magnet should never be brought to the eye. Before the conjunctival flap is sutured in place a cotton-tipped applicator dipped in pure phenol is touched to the scleral wound to prevent postoperative detachment of the retina.

In case of a fairly large piece of copper, brass, coal, stone, wood or lead shot, with the aid of a localization chart and an adequate scleral opening, the forceps (properly designed) are opened and the foreign body is removed. This may require several attempts and may damage the integrity of the eye. Small shot are now made of chilled steel and are therefore magnetic.

DISCUSSION

Dr. E. S. Sherman, Newark, N. J.: Dr. Stieren's practice of enucleating immediately every eye in which the wound of entrance involves the ciliary body is unnecessarily radical. If the eye is not blind, one should wait a week before enucleating it. In the meantime active foreign protein therapy will often give gratifying results. The fear of retinal detachment following transscleral extraction is exaggerated.

Dr. C. A. Veasey Sr., Spokane, Wash.: In cases in which the action of a foreign protein alone is desirable, typhoid vaccine is usually used. If the wound of entrance is through the ciliary body, enucleation is recommended. A few patients have refused to undergo operation and have escaped trouble, but delay is dangerous.

Dr. G. H. Cross, Chester, Pa.: Steel is now combined with many substances which render it less magnetic, so that there are more cases in which nonmagnetic foreign bodies are to be removed. There need be no groping in removal of such foreign bodies. With the assistance of a good roentgenologist and the use of the method which I devised in 1926, it is possible to apply scleral forceps and remove nonmagnetic bodies from the eye with a minimum of trauma even when no view of the interior of the eye is obtainable. When the foreign body is in the lens, sufficient time should be allowed for the lens to become thoroughly opaque, and then an intracapsular operation should be done by the Knapp method. Glass in the anterior chamber sometimes can be removed under high magnification and sharp illumination by grasping the glass fragment with a pair of fine needle point forceps.

Dr. E. Stieren, Pittsburgh: As there is no way of determining in which of the cases with injury of the ciliary body sympathetic ophthalmia may develop, one assumes a tremendous responsibility in retaining the eyeball. Even with use of the fluoroscope there must be more or less disturbance of the vitreous as the forceps are directed to move up or down, to the right or to the left.

Significance of Visual Defects in War Production Effort. H. S. Kuhn, M.D., Hammond, Ind., J. A. M. A. **123:** 1085 (Dec. 25) 1943.

A direct correlation was shown by means of graphs between accuracy and visual perfection and between accidents involving loss of time and defects in visual performance.

The minimal visual standards adopted were simple groupings of the basic visual findings according to the visual demands of job groups; they included (1) uncorrected acuity for distant and for near vision; (2) acuity with the glasses habitually worn, i. e., work acuity; (3) muscle balance for distant and for near vision; (4) stereopsis, and (5) color appreciation. To this basic, minimal information were added such special tests of near vision (e. g., determination of the near point of accommodation and of convergence) as might be needed in selecting eyes for exceedingly intricate work done within 12 inches (30 cm.) of the eye. Physicians in general have an exceedingly important and a direct responsibility in the war production effort.

DISCUSSION

Dr. H. Glenn Gardiner, Chicago: This is a graphic representation of what is probably one of the greatest rehabilitation programs brought forward during the war.

Dr. T. L. Terry, Boston: "Determination of minimal visual standards for a given occupation" is neither easy nor exact, as superior mental ability may make up for lower visual standards. Education in all mechanical means of preventing blindness is the answer to one phase of the problem.

Dr. M. Davidson, New York: The problem is the organization of effective care of the eyes for the industrial population. Educational work with industrial management is also needed to make it realize that visual defects undoubtedly account for a considerable proportion of accidents and that "carelessness," to which 50 per cent of the accidents are attributed, is also partly the result of undiscovered visual defects among the industrial workers. There is needed a program of special training for such work which would provide for departments of industrial ophthalmology in all graduate schools of ophthalmology and for the development of a standard technic of examination and standard organization of ophthalmic care in industry.

Dr. H. S. Kuhn, Hammond, Ind.: It is not necessary to start with exact determinations. Ophthalmologists can greatly assist in placement if they do such simple things as eliminate all persons who lack depth perception from the lists of prospective crane operators, power machinists, tractor drivers and the like.

Distribution of Epidemic Keratoconjunctivitis in the United States. A. J. Bedell, M.D., Albany, N. Y., J. A. M. A. **123:** 1101 (Dec. 25) 1943.

Keratoconjunctivitis is not a new disease. A number of severe and extensive outbreaks have

been reported in the literature. No race is exempt, and no particular occupation either predisposes to or is responsible for it.

The particular phase of this subject which the article discusses is the distribution of epidemic keratoconjunctivitis in the United States. A map is included which shows the location of the major outbreaks and the cities from which reports to the author were received for 1941 and 1942. An inspection of the map shows that in continental United States there have been four large outbreaks: In Portland, Ore., Rieke saw several hundred cases; in Seattle, Dawson reported hundreds of cases; in the San Francisco Bay area Nutting, Cordes, Hogan and Crawford and others treated several thousand patients, and in Schenectady, in the capital district of Albany, N. Y., thousands of persons had the disease.

The author gives the following summary and conclusions: A worldwide disease of the conjunctiva and cornea assumed epidemic proportions on the Pacific Coast and later in an inland city. The explanation of its predilection for some coastal cities in the West and its practically complete absence in similar localities in the East is something to engage the attention of the student.

Its failure to appear in any of the great army mobilization centers speaks well for the health of the men in service, as well as for the high standard of sanitation in the camps.

Keratoconjunctivitis is not a new disease. It affects young and old.

There has been no epidemic in the shipyards on the Gulf of Mexico or along the Atlantic Coast, a fact proving conclusively that it is not strictly a shipyard disease.

Because of the rush of war and the overwhelming number of cases it is possible that several diseases have been included under the term epidemic keratoconjunctivitis. It is certain that more complications and greater and more extensive ocular involvements were reported from the West Coast and Hawaii than were experienced in other parts of the country.

To infer that the epidemic spread throughout the United States is not warranted by the collected facts.

DISCUSSION

Dr. Thomas D. Allen, Chicago: This disease is not new to the world, but in the form in which it exists in the United States today it is new to ophthalmologists. The character of the disease seems to have changed, as in the Hammond, Ind., region Kuhn reported that keratitis now develops in only 10 per cent as compared with about 65 to 80 per cent at first. Any ophthalmologist who has had the disease, as I have, and has traced it to its source, as I did, would agree that it is contagious. In communities where it has suddenly gained access its control has been in direct proportion to the vigilance of the medical profession and the local boards of health. Soap and water constitute the first line of defense.

Dr. Michael J. Hogan, San Francisco: The results of Dr. Bedell's survey lead one to draw several conclusions: First, the epidemic on the Pacific Coast must have been initiated by patients who acquired the disease in the Hawaiian epidemic and carried the infectious agent to the mainland. Second, the disease first gained a foothold among ship workers and was spread rapidly among them both by close contact and by the considerable shifts in personnel which occurred during 1940 and 1941. One finds it difficult to explain the high incidence of the disease in industrial plants while the incidence in general population is relatively low. However, because of this the California State Industrial Accident Commission has ruled that the disease is compensable. The California State Superior Court has concurred in this finding. Many ophthalmologists have disagreed with this opinion.

Dr. A. J. Bedell, Albany, N. Y.: There is no justification for use of the term epidemic keratoconjunctivitis unless the cornea is involved. I approve of Dr. Hogan's disagreement with the California State Superior Court in concurring with the decision of the California State Industrial Accident Commission that the disease is compensable, "simply because the incidence of the disease was higher among shipyard workers than in the rest of the population."

Fever Therapy in Ophthalmology. F. C. Cordes, M.D., San Francisco, J. A. M. A. **124:** 14 (Jan. 1) 1944.

Injections of milk are of particular value in the treatment of infants, especially those with ophthalmia neonatorum, since the injections usually cause fever with a temperature of 100 to 103 F. This applies even though the sulfonamide compounds are used, as it has been shown that their action is greater in the presence of elevated temperatures.

Diphtheria antitoxin has many disadvantages, but its use in the treatment of sympathetic ophthalmia seems justified.

Typhoid vaccine is the most useful and generally employed agent to produce fever for the treatment of acute lesions of the eye and its adnexa. On the theory that vasodilation may

be a factor in the beneficial results, smaller doses administered over a longer period seem as effective and cause less shock and discomfort. The temperature reaction in a series of cases in which smaller doses were used corresponded closely to that obtained in a series in which the average first dose was 53,000,000 and the average second dose 80,000,000 organisms. There are certain rather definite contraindications to its use.

When a milder temperature response is indicated or the patient's condition does not warrant the use of typhoid vaccine, the employment of Coley's mixed toxins is advisable. This preparation is a mixture of toxins derived from killed cultures of Staphylococcus erysipelatis and Bacillus prodigiosus, which are grown separately, then mixed and finally diluted to a definite strength. It has the advantage that hospitalization is not necessary.

Omnadin, which consists of a mixture of protein substances obtained from nonpathogenic bacteria, various animal fats and lipids derived from bile, has a place in the treatment of acute conditions when shock therapy must be avoided but leukocytosis and a rise in the antibody content of the blood are desirable. It is not as effective as typhoid vaccine or other forms of foreign protein but can be used when they are contraindicated.

The use of malaria is not justified in treatment of ophthalmic diseases.

Hyperpyrexia induced by high frequency methods is still in the experimental stage. Further observations are necessary to disclose the conditions in which it is most effective and to establish the dosage compatible with safety.

Of the various physical means used to produce hyperpyrexia, air-conditioned cabinets of the Kettering hypertherm type are best. Production of fever by physical means is most efficacious in the treatment of gonorrheal conjunctivitis and syphilitic keratitis and iridocyclitis. It is particularly useful in the treatment of syphilitic diseases of the eye. Because of the severity of the treatment, it should be used only in cases in which other forms of therapy are unsatisfactory.

DISCUSSION

Dr. E. L. Goar, Houston, Texas: In recent years I have confined my efforts in fever therapy to the intravenous use of typhoid H antigen. This agent is preferred because it produces the same therapeutic results as the mixed vaccine, with less discomfort. This is the best treatment for anterior uveitis which is not of tuberculous or syphilitic origin. It is much less efficacious with posterior uveitis and is of doubtful value with optic neuritis.

Dr. S. R. Gifford, Chicago: In cases of acute iridocyclitis in the absence of syphilis the evidence of a bacterial agent is often wanting, while an exact bacteriologic diagnosis is usually impossible. Foreign protein therapy, with or without the sulfonamide compounds, is of considerable value. Typhoid vaccine administered by vein in the dosage recommended by Allen, 30,000,000 to 80,000,000 organisms, usually produces the desired effect. In cases of optic neuritis and retrobulbar neuritis large doses of thiamine hydrochloride are added. Hyperpyrexia by physical means has a definite place in the treatment of those forms of syphilis which are resistant to chemotherapy alone.

Dr. Grady Clay, Atlanta, Ga.: In the clinic, boiled milk is used, with good results. In private practice, I employ subcutaneous injections of a milk preparation and intravenous injections of typhoid vaccine. In every case in which intraocular operation is performed intramuscular injections of a foreign protein are given. They are used in all cases of bacteria-infected corneal ulcer, in all cases of intraocular inflammation and for severe types of optic neuritis, especially when associated with encephalitis.

Dr. F. C. Cordes, San Francisco: I agree with Dr. Gifford that sulfonamide compounds are so effective in treatment of ophthalmia neonatorum that milk injections are probably unnecessary. I agree with Clay that typhoid vaccine should not be given in the office or at home because of the possible reactions that may at times be encountered in its use.

Chemotherapy in Ophthalmology. P. Heath, M.D., Detroit, J. A. M. A. **124:** 152 (Jan. 15) 1944.

When several agents are equally effective in meeting a problem, low toxicity and freedom from sensitization reactions or late harmful effects should govern the selection. The effective dose and concentration vary with different infections and different patients. In treatment of inclusion blennorrhea, sulfathiazole was used internally and locally. Gonorrheal ophthalmia or conjunctivitis are effectively treated with oral doses of sulfapyridine, sulfathiazole or sulfanilamide, ice compresses for any considerable edema (occasionally canthotomy), antiseptic irrigations and an ointment containing a sulfonamide compound. Therapy of hemolytic staphylococcus conjunctivitis consists of the administration of staphylococcus toxoid and local application of

antiseptic lotions and a sulfonamide ointment. For pneumococcic conjunctivitis (except that due to the Friedländer type) tyrothricin is used. In treatment of pneumokeratitis the oral administration of a sulfonamide compound is added. In the management of severe traumatic injuries general chemotherapy is necessary. In cases of epidemic keratoconjunctivitis the most favorable results have been obtained with tyrothricin. In cases of keratitis and ulcer due to Bacillus pyocyaneus, early treatment with sulfapyridine or sulfadiazine is indicated. Treatment of dendritic keratitis by local application of tyrothricin, with repeated pasteurization by cautery, has led to the most rapid cure. Blepharitis and the form of punctate keratitis associated with chronic conjunctivitis are sometimes cured by use of sulfonamide ointments; tyrothricin and the disease compound neo-synephrine sulfathiazolate has relieved some obstinate forms of the disease. In treatment of orbital abscess one of the sulfonamide compounds, hot compresses and drainage are employed. With thrombosis of the cavernous sinus a high dosage of sulfadiazine is used. In cases of uveitis the causative agent is attacked. Sulfonamide compounds may be of value. In treatment of trachoma sulfanilamide is the drug of choice. The drug reduces secondary infections and causes improvement in corneal involvement. The progress of postoperative infection may be checked by the use of sulfadiazine or sulfapyridine. With low grade dacryocystitis irrigation with a solution of tyrothricin through the lacrimal sac is indicated.

DISCUSSION

Dr. Alan C. Woods, Baltimore: I am in general agreement with Dr. Heath as to the value of the sulfonamide compounds, but my results with tyrothricin have not been so happy. In treatment of recurrent iritis, tuberculous uveitis, choroiditis and sympathetic ophthalmia, the use of sulfonamide compounds has repeatedly been without favorable therapeutic effects. The present indication is that penicillin will probably be the most effective agent against infection with the gram-positive organism.

Dr. W. S. Atkinson, Watertown, N. Y.: The nonspecific use of sulfonamide compounds should be avoided, and their local use in postoperative medication is contraindicated.

Dr. J. G. Bellows, Chicago: The sulfonamide compounds must be used with caution in treatment of traumatic lesions of the cornea because in the absence of normal epithelium they cause severe injury. In the treatment of epidemic keratoconjunctivitis "sulfathiazole desoxyephedrine" reduces rapidly the subjective symptoms and the redness and swelling, without influencing the scarring.

Dr. R. C. Gamble, Chicago: In cases of sympathetic ophthalmia the sulfonamide compounds hold the progress of the disease in check, giving time for the natural healing processes of the ocular tissue to act.

Industrial and Domestic Injuries of the Eye. C. P. Clark, M.D., Indianapolis, J. A. M. A. **124:** 157 (Jan. 15) 1944.

The author gives the following summary:

The prevention of ocular injuries commands an important place in industry, agriculture and the home.

Efficient first aid treatment is important in reducing the loss of man hours of work, in relieving the suffering associated with the injury and, most important of all, in retaining useful vision of the injured eye.

Penetrating and nonpenetrating wounds are treated according to the rules which years of experience of members of the medical profession have proved best.

Particular care should be taken to avoid sympathetic ophthalmia when there has been an injury of the uveal tract, especially of the ciliary body.

DISCUSSION

Dr. W. F. Holzer, Worcester, Mass.: In my community most injuries are foreign bodies in the cornea or abrasions of the cornea. My practice is to remove the foreign body, curet the cornea thoroughly, cauterize with 95 per cent phenol and leave the eye uncovered. Sulfathiazole (5 per cent ointment) is applied to the lower cul-de-sac, and a tube of ointment containing 1 per cent phenacaine hydrochloride and epinephrine (1:50,000) is dispensed, to be used every hour or two as required.

Dr. H. L. Blair, Rochester, Minn.: A common error is the failure to remove early enough of the blood clot that fills the anterior chamber after contusion. Many such eyes have been lost, owing to hematogenous infiltration of the cornea and secondary glaucoma. There is overuse of the conjunctival flap for penetrating laceration of the cornea. The larger corneal lacerations should be closed with corneal sutures ¼ inch (0.6 cm.) apart.

Dr. E. W. Griffey, Houston, Texas: A simple and effective remedy for flash burns of the eye after exposure to the welder's arc, which in

the initial phase amounts to good prophylaxis, is the use of three successive instillations of 1:1,000 solution of epinephrine hydrochloride at five minute intervals shortly after onset of ocular pain following flash burn, and before objective signs are too obvious.

Dr. Albert C. Snell, Rochester, N. Y.: In industry, adequate provisions for rendering such aid should be available in every plant, both large and small. These provisions should include proper equipment and supplies, as well as definite written instructions to be followed by the available personnel. In my opinion, small or medium-sized prolapsed parts of the ciliary body should be amputated thoroughly, but one should always be alert to the possibility of sympathetic involvement. In minor degrees of prolapse of the choroid, usually with some vitreous, amputation should be done and prophylactic treatment employed.

Dr. C. P. Clark, Indianapolis: The subject can be summarized briefly: an aggressive educational campaign to prevent accidents where they are most likely to occur; prompt and efficient emergency care for the injured, and employment of good ophthalmic surgical practice for persons more seriously injured. The methods for accomplishing these aims may vary according to the locality and the facilities that are available.

1930 Chestnut Street.

Book Reviews

Manual of Diseases of the Eye. By Charles H. May, with the assistance of Charles A. Perera. Eighteenth Edition. Price, $4. Pp. 520, with 387 illustrations, including 32 plates and 93 colored figures. Baltimore: William Wood & Company, 1943.

The present edition, appearing three years after the preceding one, has been revised and brought up to date. The chapters "Lacrimal Apparatus" and "Errors of Refraction" have been rewritten. The latter has been contributed by Dr. Alson E. Braley, assistant professor of ophthalmology, Columbia University College of Physicians and Surgeons.

Among the changes made in this revision, mention should be made of the following two: compensation for ocular eye injuries and the requirements for admission to the military services of the Army of the United States.

The book remains in this revised edition a most reliable manual of instruction for the student and the general practitioner.

Arnold Knapp.

Studies from the School of Medicine, the George Washington University for 1942-1943. Washington, D. C., 1943.

Under this title, 43 reprints have been bound together to represent the literary output for 1942 and 1943. A great variety of subjects are included, and the various departments of the university are ably represented. From the department of ophthalmology the director, Dr. W. T. Davis, has contributed the following two articles: "Differential Diagnosis of Paresis of the Oblique and the Superior and Inferior Recti Muscles" (*Tr. Am. Acad. Ophth.* **47**:206, 1943) and "Differential Diagnosis of the Tropias, with Special Reference to the Value of Orthoptic Training" (*Am. J. Ophth.* **25**:697, 1942).

Arnold Knapp.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Comparative Ophthalmology

CHOLINE ESTERASE AT THE NERVE TERMINATION IN THE SPHINCTER PUPILLAE OF THE TURTLE. P. B. ARMSTRONG, J. Cell. & Comp. Physiol. 22: 1 (Aug.) 1943.

Experiments on preparations of the iris of the young Cumberland tortoise (Pseudemys elegans), which possess a striated sphincter pupillae, led to results which differed distinctly from those which the author reported for amphibian eyes. The responses of this muscle to stimulation with acetylcholine, physostigmine, nicotine, atropine and the electric current through the afferent nerve fibers were similar to those of the superior cervical ganglion of the cat, reported by Feldberk and Vartiainen, and to those of the striated sphincter iridis of the bird, reported by Dale. They showed high thresholds for acetylcholine and marked potentiation by physostigmine. High concentrations of atropine were necessary to reduce the response to acetylcholine. The initial stimulation of the sphincter with nicotine was followed by paralysis. This group of responses of the sphincter iridis of the tortoise characterizes the "nicotine" action of acetylcholine, whereas the "muscarine" effects are evident in the amphibian sphincter pupillae. In contrast to the latter, high concentrations of choline esterase appeared to be present in the afferent nerve terminations of the sphincter pupillae of the tortoise.

L. VON SALLMANN.

General Diseases

TEMPORAL ARTERITIS. L. T. POST and T. E. SANDERS, Am. J. Ophth. 27:19 (Jan.) 1944.

Post and Sanders report the case of a housewife aged 66 who came under observation because of failing memory and mental deterioration. The left temporal artery was prominent, thickened and tortuous and the surrounding tissue hyperemic. A section of the right temporal artery, which showed similar changes, was removed for examination, and definite changes were noted. The retinal arteries showed pronounced sclerosis, with irregularity of caliber and thickening of the walls, and in places sheathing. The patient died suddenly of a cerebral hemorrhage. The authors discuss temporal arteritis. They believe that no particular ocular lesion is characteristic.

W. S. REESE.

Glaucoma

NEVUS FLAMMEUS ASSOCIATED WITH GLAUCOMA: REPORT OF A CASE IN WHICH CYCLODIATHERMY WAS USED IN AN ATTEMPT TO CONTROL THE INTRAOCULAR PRESSURE. B. Y. ALVIS and V. A. TOLAND, Am. J. Ophth. 26: 720 (July) 1943.

A boy aged 14 years had a naevus flammeus on the right side of the face which conformed in outline with the cutaneous distribution of the ophthalmic and maxillary branches of the right trigeminal nerve. The nevus was also present on the mucous membranes of the nose and throat and followed the same distribution. The right eye showed hydrophthalmos, with a tension of 43 mm. of mercury (Schiøtz). There was deep, glaucomatous cupping of the optic nerve. A corneoscleral trephine was done, but the opening closed. Vogt's cyclodiathermy was then carried out. About six months later the tension was 16.5 mm. of mercury, and corrected vision was 5/75. A Bjerrum scotoma was present in the field of vision.

W. ZENTMAYER.

Hygiene, Sociology, Education and History

ASPECTS OF BRAZILIAN OPHTHALMOLOGY. M. E. ALVARO, Am. J. Ophth. 26: 474 (May) 1943.

Alvaro traces the progress of ophthalmology in Brazil and describes the present day management of certain diseases of the eye that are encountered in that country. A board of ophthalmology is now operating in Brazil.

W. ZENTMAYER.

REHABILITATION OF THE UNI-OCULAR PATIENT. C. G. SCHURR, Brit. J. Ophth. 27: 467 (Oct.) 1943.

It is desirable that active steps to reeducate the disabled be taken as soon as possible and such reeducation may commence within a day or two of the removal of the eye.

Schurr gives an account of the methods employed in cooperation with the rehabilitation department of the Royal Sussex County Hospital. The treatment is both physiologic and psychologic.

W. ZENTMAYER.

Injuries

A Case of Removal of Non-Magnetic Foreign Body from the Ciliary Region. D. Pierse, Brit. J. Ophth. 27: 550 (Dec.) 1943.

Following the technic of Spaeth, Pierse removed a piece of brass from the ciliary region. An attempt was first made to remove the foreign body through a corneal incision; as a result, it disappeared backward through the hole in the iris. A needle was inserted at the estimated position of the foreign body, and its exact location was determined by a roentgenogram. A trap door opening, with the hinge of the flap at the limbus, was made in the sclera, and the foreign body was easily removed through the ciliary body. Pierse comments that had a roentgenogram been taken immediately the attempted removal through the cornea would have been averted.

The article is illustrated. W. Zentmayer.

Methods of Examination

Further Observations on Autofundoscopy (Auto-Ophthalmoscopy of Eber; Purkinje Figure of Walker). L. C. Drews, Am. J. Ophth. 26: 1143 (Nov.) 1943.

Drews draws the following conclusions:

"1. Widening of the afterimage of the filaments, as seen with my slightly myopic eye, is due chiefly to chromatic aberration.

"2. An apparatus for measuring muscle balance or for determining the presence of normal retinal correspondence can be made by simply mounting a strong plus cylinder on a paper tube of a length equal to the focal length of the cylinder and stretching a heavy rubber band across the cylinder between the axis marks. With a second tube, similarly prepared, it is possible to study binocular afterimages simultaneously produced.

"3. The decrease in size of the optic disc as seen by autofundoscopy probably is due to the 'filling up of the blind spot.'

"4. Scotomas in the central 10 degrees of the field do not show any appreciable tendency toward 'filling up,' as is evidenced by accurate measurement of these scotomas by autofundoscopy.

"5. Autofundoscopy requiring flooding of the eye with light may make it possible to visualize a paracentral area of the retina where retinal function is normal, except that regeneration of visual substance is delayed (case 5). This is wholly hypothetic.

"6. If a scotoma in the central 10 degrees of the field did show 'filling up' comparable to the filling of the scotoma of the optic nerve, it would be seen with autofundoscopy to be much smaller than it really is. Do congenital scotomas due, for instance, to coloboma of the choroid, show this?" W. S. Reese.

Neurology

Changes in the Eyes in Amaurotic Family Idiocy (Infantile Type of Tay-Sachs Disease): Histopathologic Observations in a Case. G. Hassin, Arch. Neurol. & Psychiat. 49: 628 (April) 1943.

"The eyes, together with the brain and spinal cord, in a typical case of amaurotic family idiocy, were removed sixteen hours after death.

"The following conclusions are drawn from the study of this material:

"1. The changes in the retina and optic nerves in patients suffering from amaurotic family idiocy are analogous to the changes in the central nervous system in general.

"2. The perioptic spaces exhibit the presence of elements similar to those seen in the subarachnoid spaces of the brain and spinal cord.

"3. The hyperplasia of the pial septums in the optic nerves is analogous to that of the pia-arachnoid and is a reaction of the latter to the presence of abnormal products of activity of the ganglion cells discharged there by way of the perioptic spaces.

"4. Status spongiosus—a manifestation of severe destruction of nerve tissue—is a striking feature in the changes in the optic nerve associated with amaurotic family idiocy."

R. Irvine.

Integrated Facial Patterns Elicited by Stimulation of the Brain Stem. E. Weinstein and M. Bender, Arch. Neurol. & Psychiat. 50: 34 (July) 1943.

"The facial patterns as they occur normally in the monkey and in man are both voluntary and involuntary. They resemble automatic, stereotyped movements, such as walking or swimming, which to a considerable degree are performed unconsciously. The question is where these facial movements are integrated in the nervous system. According to Ranson, the subthalamus serves as a regulator and coordinator of such somatic functions. Direct stimulation of the subthalamus has indicated (Bard; Hinsey) that this structure is an integrating center for both the somatic and the visceral components of emotional expression, efferent paths making connections with the primary motor nuclei of the brain stem and the spinal cord. However, in our experiments stimulation of the monkey's hypothalamus failed to produce any coordinated facial expressions unless currents stronger than those previously described were used. Furthermore, there is no reason to believe that our responses from the brain stem were elicited from descending hypothalamic pathways. On the basis of our experiments, it seems that the brain stem is an important integrator of somatic functions of the cranial muscles.

"Stimulation of designated areas in the tegmentum of the brain stem of the macaque monkey with the Horsley-Clarke stereotaxic technic produces facial patterns integrated with other somatic and automatic components into purposeful acts.

"The facio-ocular synkinesis of contraction of the orbicularis oculi muscles, upward rolling of the eyeballs and constriction of the pupils can be elicited from the reticular substance of the pons 1.5 to 2.5 mm. lateral to the midsagittal plane.

"Contraction of the orbicularis oris muscle in a sucking, swallowing movement is associated with elevation of the base of the tongue, raising of the uvula and inhibition of respiration in the inspiratory phase. This pattern is elicited from the reticular formation of the medulla 0.5 to 1.5 mm. from the midsagittal plane dorsomedial to the rostral part of the inferior olive.

"A faciorespiratory complex simulating laughter and consisting of retraction and elevation of the corners of the mouth, depression of the lower jaw, lowering of the base of the tongue and uvula and cessation of respiration in the expiratory phase can be elicited from an area 0.5 to 2 mm. from the midsagittal plane dorsomesial to the inferior olive.

"It is suggested that the facio-ocular and faciorespiratory synkinesias are integrated in the reticular formation of the brain stem."

R. IRVINE.

TUBEROUS SCLEROSIS. A. ROSS and W. DICKERSON, Arch. Neurol. & Psychiat. **50:** 233 (Sept.) 1943.

This unusual disease is congenital and may be hereditary or familial. The clinical material on which this paper is based was derived from the study of 25 patients. The basic characteristics of tuberous sclerosis are developmental anomalies in tissues of ectodermal origin, particularly the brain, skin and retina; defective development and tumor formation are not infrequently manifested elsewhere.

The usual clinical criteria for the recognition of tuberous sclerosis are adenoma sebaceum on the face, retinal tumors, mental deficiency and convulsions, although it is not necessary for all these qualifications to be fulfilled in order that the diagnosis be established. At times sebaceous adenoma is the only sign of the disorder. The retinal lesions, as a rule, consist of whitish gray nodules (phakomas), which may be single or multiple, flat or raised, may be situated anywhere on the fundus and ordinarily are not directly connected with blood vessels.

Six patients in the series had retinal tumor, in 1 of whom the lesion was bilateral. In 4 patients the tumor appeared either to have its origin at the margin of the disk or to cover the major portion of the disk itself. In the 2 remaining patients the involved area was situated above and temporal to the disk.

An autopsy in 1 case with involvement of the eye is reported in detail. The retinal nodules were areas of gliosis composed of cells of a type not entirely clear, but probably astrocytic or astroblastic. This adds support to the theory of the glial origin of the tumor.

R. IRVINE.

STUDIES IN DISEASES OF MUSCLE: XIV. PROGRESSIVE MUSCULAR ATROPHY OF PERONEAL TYPE ASSOCIATED WITH ATROPHY OF THE OPTIC NERVES; REPORT ON A FAMILY. A. MILHORAT, Arch. Neurol. & Psychiat. **50:** 279 (Sept.) 1943.

The occurrence of progressive peroneal muscular atrophy associated with progressive bilateral optic nerve atrophy in 2 brothers is described. Cases of a similar disease in 8 members of 6 families were reported previously, with 2 other members having typical muscular changes but no visual disturbance. All the patients were males; the occurrence of the syndrome in females appears not to have been observed. A sister of the 2 patients described in this report had bilateral optic nerve atrophy and a disease which most probably was disseminated sclerosis. The relation, if any, between the condition in the brothers and that in the sister is at present not understood. It appears likely that the syndrome described in this report represents either a clinical entity which is different from the muscular conditions usually recognized or a definite form of progressive peroneal muscular atrophy.

R. IRVINE.

Ocular Muscles

THE PARENTS' ROLE IN ORTHOPTIC TRAINING. F. WALRAVEN, Am. J. Ophth. **26:** 1175 (Nov.) 1943.

Walraven gives the following summary:

"The parents should understand fully the following points:

"1. Sufficient knowledge of binocular vision is essential.

"2. The time necessary for the developing of binocular vision varies with the individual.

"3. In selected cases of amblyopia, occlusion is always necessary.

"4. The child's response to occlusion largely depends on the attitude of the parents.

"5. Home exercises must be thoroughly understood before they are practiced.

"6. Stimulation is necessary for the required mental effort.

"7. Surgery cannot accomplish alone what it does in conjunction with orthoptic training.

"8. Full cooperation with ophthalmologist and technician is necessary to a successful training period."

W. S. REESE.

A Method of Evaluation of Binocular Muscle Balance. D. D. S. Stewart, Brit. J. Ophth. **27**: 477 (Nov.) 1943.

Stewart describes a rapid method of estimating, as a part of the routine ophthalmic examination, the dynamic ocular equilibrium for distance. He believes that daily familiarity with the variability of functions concerned with binocular muscle balance and their association with visual comfort will reconcile prevalent exaggerated skepticism and enthusiasm about the whole subject.

The article is illustrated. W. Zentmayer.

Operations

Improved Technique for Implantation of a Ball in Tenon's Capsule. F. H. Verhoeff, Am. J. Ophth. **26**: 1057 (Oct.) 1943.

The conjunctiva is incised close to the limbus and then, with all the underlying tissue down to the sclera, is carefully dissected from the globe; at this stage the conjunctiva is not dissected from Tenon's capsule. After removal of the eye, the glass ball is inserted and pushed back in the orbit. Tenon's capsule is grasped near the cut end of the tendon of the external rectus muscle, and a tongue, consisting of two layers of the capsule, is pulled forward. About 5 mm. behind the end of the tongue two needles of a double-armed catgut suture are passed through the tongue from beneath, the vertical distance between them being about 6 mm. The two needles are then passed from beneath through a similar tongue in front of the tendon of the internal rectus muscle. Then they are passed from beneath a tongue in front of the superior rectus muscle, one in front of the other, the upper being about 7 mm. behind the end of the tongue and the lower about 3 mm. farther back. The needles are then passed through a tongue in front of the tendon of the inferior rectus muscle, the lower needle being the one farther back. The ends of the sutures are then pulled on until all four tongues are brought together in front of the ball. The suture is then tied securely and cut close to the knot. The conjunctival opening is closed horizontally by a continuous silk suture. At the completion of the operation a form is placed in the conjunctival sac.

W. Zentmayer.

Physiology

Fusion, Projection, and Stereopsis. I. Franklin, Am. J. Ophth. **25**: 1316 (Nov.) 1942.

Stereopsis, fusion and projection are not purely sensory or sensory-psychic abstractions, but are eye-limb-body, locomotion and prehension functions, in which the body and limb movements have evolved from an actual to a potential form.

W. S. Reese.

Clinical Vascular Physiology of the Eye. W. F. Duggan, Am. J. Ophth. **26**: 354 (April) 1943.

Duggan discusses a number of retinal and other lesions, the results of homeostatic reactions which are physiologic in nature but pathologic in degree. Many of these lesions have been attributed to toxins, foci of infection and allergy. All can be interpreted as due to variations in the arterioles and capillaries which differ quantitatively from the normal. The cause is usually endogenous. W. Zentmayer.

Refraction and Accommodation

High Congenital Myopia with Convergent Strabismus. R. C. Gamble, Am. J. Ophth. **27**: 159 (Feb.) 1944.

Gamble draws the following conclusions:

"1. High congenital myopia and convergent strabismus are often associated.

"2. The myopia is lenticular in origin and relatively nonprogressive, at least up to the age of adolescence.

"3. The convergent strabismus is of low degree, is usually corrected by glasses, and is, on the whole, relatively unimportant."

W. S. Reese.

A New Approach to Cross Cylinder Tests. J. I. Pascal, New York State J. Med. **43**: 323 (Feb. 15) 1943.

This article discusses the chief difficulty in application of cross cylinder tests, which is the fact that the patient often has to compare images made up of diffusion spots of different shapes, as well as of different sizes. Thus, he frequently has to say that the letters in the two positions of the cross cylinder are blurred about equally, but in a different way. The article explains the reasons for this behavior and develops a method of using cross cylinders so that this difficulty is eliminated.

It is possible to apply cross cylinders for testing and correcting astigmatism in the same way as spherical lenses are used for testing and correcting hyperopia and myopia. The same charts can be used, and, what is especially significant, the changes produced in the patient's retinal images are the same as those produced during a test for a spherical error. The procedure is to change the astigmatism to equally mixed astigmatism and maintain it thus throughout the test by the use of correcting cross cylinders. In this way, the patient will have to compare images made up of diffusion circles of different sizes, exactly as he does during a test with spherical lenses for a spherical error.

W. Zentmayer and J. I. Pascal.

Uvea

ENDOPHTHALMITIS DUE TO B. SUBTILIS FOLLOWING INJURY. A. B. REESE and D. KHORAZO, Am. J. Ophth. **26:** 1251 (Dec.) 1943.

Reese and Khorazo report the case of a man aged 56 in whom acute iridocyclitis with hypopyon followed an injury from an intraocular foreign body. The eye was enucleated. Bacillus subtilis was present which was not pathogenic for guinea pigs but induced endophthalmitis when injected into the anterior chamber of a rabbit's eye.

W. S. REESE.

IRIDO-CYCLITIS AND CHOROIDITIS DUE TO "SILENT" SINUSITIS. R. FORD, Brit. J. Ophth. **27:** 469 (Oct.) 1943.

The author cites the histories of 2 patients to show how elusive, even with every advantage for expert diagnosis, the cause of uveitis may be; she also gives the histories of 3 other patients to demonstrate that elimination of a focus of infection in the sinuses, even when there is no evidence of its existence other than the uveitis, may lead to prompt and permanent cure. She concludes that if all investigations prove negative in a case of uveitis, latent sinusitis should be suspected and treated.

W. ZENTMAYER.

VOGT-KOYANAGI SYNDROME. L. J. MONTALVO DURAND, Bol. Asoc. Méd. de Puerto Rico. **35:** 218 (June) 1943.

According to Montalvo Durand, the Vogt-Koyanagi syndrome is rare. The most important symptoms are nontraumatic bilateral uveitis; premature graying; alopecia; symmetric vitiligo, especially on the hands, wrists and feet, and dysacousia. The cause is unknown. Japan is the place of greatest incidence. The disease develops most frequently in persons between 30 and 40 years of age. Syphilis and tuberculosis have a certain contributory significance in the development of the disease.

J. A. M. A. (W. ZENTMAYER)

Therapeutics

INTRAOCULAR INJECTION OF SULFANILAMIDE IN A CASE OF PURULENT IRIDOCYCLITIS. J. IGERSHEIMER, Am. J. Ophth. **26:** 1045 (Oct.) 1943.

In a case of purulent iridocyclitis traumatica enucleation was planned because of great irritation and absence of sensitivity to light. After injection of sulfanilamide into the anterior chamber inflammation disappeared, and final vision was 20/40.

W. ZENTMAYER.

X-RAY THERAPY OF INFLAMMATORY AND NEOPLASTIC DISEASES OF THE EYE. J. BORAK, Am. J. Ophth. **26:** 1170 (Nov.) 1943.

Borak refers briefly to the radiosensitivity of the different tissues of the eye and to lesions amenable to roentgen ray therapy, giving a list of these lesions and the effect of treatment.

W. S. REESE.

News and Notes

GENERAL NEWS

Postponement of Second Pan-American Congress of Ophthalmology.—The second Pan-American Congress of Ophthalmology, which was scheduled to be held in November 1944 in Montevideo, Uruguay, has been postponed until the fall of 1945, particularly because of transportation difficulties.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, China.

Chinese Ophthalmology Society

Presdient: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

Ophthalmological Society of the United Kingdom

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Place: Oxford, England. Time: July 8-9, 1943.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4. Warsaw.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President: Dr. W. Belfort Mattos, Caixa Postal, 4086, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santa Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive. All correspondence should be addressed to the President.

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York City.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
Place: Chicago. Time: June 12-16, 1944.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Lawrence T. Post, Metropolitan Bldg., St. Louis.
President-Elect: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
Executive Secretary-Treasurer: Dr. William L. Benedict, 101-1st Ave. Bldg., Rochester, Minn.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. John Green, 3720 Washington Ave., St. Louis.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. R. Evatt Mathers, 34½ Morris St., Halifax, N. S.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.
Place: Halifax, N. S. Time: Aug. 4-5, 1944.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Paul A. Chandler, 5 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. L. L. Bull, 1215-14th Ave., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. H. Pike, Midland, Mich.
Secretary-Treasurer: Dr. R. H. Criswell, 407 Phoenix Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Ray Parker, 218 Franklin St., Johnston, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. C. A. Ringle, 912-9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 526 Walton St., Macon.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. J. K. Von Lackum, 117-3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Val H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings, Mont.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr B. E. Failing, 31 Lincoln Park, Newark.
Secretary: Dr. George Meyer, 410 Haddon Ave., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. James E. McAskill, 508 Woolworth Bldg., Watertown.
Secretary: Dr. Harold J. Joy, 504 State Tower Bldg, Syracuse 2.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. L. Diven, City National Bank Bldg., Bismarck.
Secretary-Treasurer: Dr. A. E. Spear, 20 W. Villard, Dickenson.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St, San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave, Dallas.

Utah Ophthalmological Society

President: Dr. R. B. Maw, 699 E. South Temple, Salt Lake City.
Secretary-Treasurer: Dr. Charles Ruggeri Jr., 1120 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. William B. Agan, 1 Nevins St., Brooklyn.

Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn.

Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. Walter F. King, 519 Delaware Ave., Buffalo.

Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.

Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.

Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.

Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.

Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago.

Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.

Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.

Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. Shandor Monson, 1621 Euclid Ave., Cleveland.

Secretary: Dr. Carl Ellenberger, 14805 Detroit Ave., Cleveland.

Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.

Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.

Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. H. D. Emswiler, 370 E. Town St., Columbus, Ohio.

Secretary-Treasurer: Dr. D. G. Sanor, 206 E. State St., Columbus, Ohio.

Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. Arthur Padillo, 414 Medical Professional Bldg., Corpus Christi, Texas.

Secretary: Dr. Edgar G. Mathis, 815 Medical Arts Bldg., Corpus Christi, Texas.

Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Abell Hardin, Medical Arts Bldg., Dallas, Texas.

Secretary: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas, Texas.

Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.

Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.

Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Dr. Raymond S. Goux, 545 David Whitney Bldg., Detroit 26.

Secretary: Dr. Arthur Hale, 1609 Eaton Tower, Detroit.

Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month, November through April.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave. Detroit.

Secretary: Dr. Leland F. Carter, 1553 Woodward Ave. Detroit.

Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.

Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.

Time: Third Wednesday in October, November, March, April, May and June.

Eastern Pennsylvania Association of Eye, Ear, Nose and Throat Physicians

President: Dr. James E. Landis, 232 N. 6th St., Reading.

Secretary-Treasurer pro tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.

Time: Last week in April each year.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.

Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.

Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.

Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.

Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.

Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.

Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.

Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.

Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.

Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.

Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. M. E. Trainor, 523 W. 6th St., Los Angeles.

Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time. 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.

Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Edwin C. Bach, 324 E. Wisconsin Ave., Milwaukee.

Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.

Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.

Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.

Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.

Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.

Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.

Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashvile, Tenn.

Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.

Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Oto-laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.

Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.

Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Frank C. Keil, 660 Madison Ave., New York.

Secretary: Dr. Willis S. Knighton, 121 E. 61st St., New York.

Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Milton Berliner, 57 W. 57th St., New York.

Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.

Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.

Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.

Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. D. D. Stonecypher, Nebraska City, Neb.

Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.

Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.

Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.

Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.

Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.

Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. John B. McMurray, 6 S. Main St., Washington, Pa.

Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.

Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. R. M. Brickbauer, Shillington, Pa.

Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.

Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.

Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.

Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.

Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. C. C. Beisbarth, 3720 Washington Blvd., St. Louis.

Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd., St. Louis.

Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.

Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.

Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.

Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.

Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.

Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.

Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. E. W. Campbell, 316 Michigan St., Toledo, Ohio.
Secretary: Dr. L. C. Ravin, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. S. Bockoven, 1752 Massachusetts Ave., Washington, D. C.
Secretary-Treasurer: Dr. John Lloyd, 1218–16th St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.

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EVALUATION OF OCULAR ANGIOSPASM

SANFORD R. GIFFORD, M.D.†

CHICAGO

Pendulums, as is well known, have a way of swinging. When an idea has served to explain one condition satisfactorily, the attempt is invariably made to use it for other purposes, and the pendulum is set in motion. The concept of angiospasm is by no means new, but the attempt to explain a number of pathologic ocular conditions as due to that entity is largely an effort of recent years. My own interest in the subject began with a study of Krogh's [1] work on the capillaries, originally published in Müller's atlas [2] (1922), and some applications of this work to ocular conditions by Scheerer, Parrisius and Mayer-List,[3] in the University of Tübingen. Out of this work arose the concept of a vasoneurotic diathesis. When the peripheral circulation was studied by various methods, certain persons were found to have an abnormally labile vasomotor system. In response to various stimuli, especially cold, to certain drugs, such as nicotine, and, in some cases, to certain foreign proteins, these persons showed signs of spasm involving the peripheral vessels, with resulting stasis in the capillary circulation. The capillaries themselves, although devoid of a true muscular coat, are narrowed, as Krogh has shown, by contraction of the Rouget cells in their walls, and in persons with vasoneurotic diathesis such contractions are easily provoked and are abnormally pronounced and prolonged.

In the earlier work reliance was placed chiefly on capillary microscopy, and patients with various ocular conditions were studied by this method. It was thought at first that patients with glaucoma often showed signs of the vasoneurotic diathesis; but the evidence was by no means convincing, and Mielke [4] noted no such relationship in his series. Attempts were made by Scheerer and others to determine vasoneurotic signs by a study of entoptic phenomena, but these efforts were not particularly successful.

As the study of peripheral vascular diseases has progressed, a series of observations and tests have been developed which determine with a fair degree of accuracy which patients have a pathologic degree of peripheral angiospasm. Dr. Gilbert Marquardt has furnished me with information concerning these special methods of examination, and he, as well as Dr. Géza de Takats, Dr. Theodore Van Dellen and Dr. J. F. Mallach, supplied me with data on patients sent them for examination. Few ophthalmologists are qualified to make these examinations, and it is unfortunately true that many internists are not sufficiently interested in the subject to provide the desired information. The examination should include a careful history. Patients with vasoneurotic diathesis usually note undue distress on exposure of the extremities to cold. Their hands become white when elevated and flushed, or even cyanotic, when dependent. They take particular care to protect the extremities against cold so as to avoid various unpleasant symptoms.

Examination should really be carried out in an air-conditioned room, but it is usually sufficient if the room is free from drafts and the patient is allowed to rest in such a room for a half-hour before examination. This precaution is taken to avoid the rapid changes which occur in persons with vasoneurotic disturbances when exposed to changes in temperature. Observation of the extremities confirms the statements in the history. The hands and feet are pale, and readings with a skin thermometer show an abnormal difference between the oral temperature and the temperature of the extremities. A difference of 3 or 4 degrees (F.) is normal, while vasoneurotic persons show differences as high as 10 degrees. The use of nicotine, as in smoking a cigaret, will cause a further drop in the peripheral temperature of susceptible persons of 6 to 12 degrees (F.). Normal persons may show a drop of 4 to

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† Dr. Gifford died February 25.

From the Department of Ophthalmology, Northwestern University Medical School.

Read at the Forty-Eighth Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 10-13, 1943, Chicago.

1. Krogh, A.: The Anatomy and Physiology of Capillaries, New Haven, Yale University Press, 1922.
2. Müller, O.: Die Kapillaren der menschlichen Korperoberfläche in gesunden und kranken Tagen, Stuttgart, Ferdinand Enke, 1922.
3. Scheerer, R.: Zentralbl. f. d. ges. Ophth. **29**:257, 1933. Scheerer, R.; Parrisius, W., and Mayer-List, R.: Klin. Monatsbl. f. Augenh. **73**:29, 1924.
4. Mielke, S.: Arch. f. Augenh. **110**:236, 1936.

5 degrees (F.) under these conditions. In 1 of our patients this drop amounted to 13 degrees (F.). Oscillometric readings are low. The pulse in one or both posterior tibial arteries may be weak or imperceptible. Microscopic study of the capillaries of the nail folds shows narrowing of the arterial limb of the capillary loops, with stasis, small aneurysms and hemorrhages in a number of areas.

When these tests have been completed and the temperature of the extremity has returned to the original level, blocking of the posterior tibial nerve is employed in patients with signs of spasm. In patients without organic changes in the vessels, a group which includes most of the younger patients with this disturbance, the temperature rises after nerve block so as to approximate the oral temperature. In patients with arteriosclerotic or thrombophlebitic changes the rise in temperature is less, or may be absent.

The blood pressure of the younger patients in the vasoneurotic group is low or normal. After the cold pressor test (dipping the hand in ice water) little, or no, rise in blood pressure occurs. When a rise of pressure does occur, the condition is considered to be early or latent hypertension, and hence in a different category from the vasoneurotic disturbance in which my colleagues and I have been most interested. The factor of peripheral spasm in patients with hypertension is of great importance, but I wish to emphasize the fact that a number of young persons show severe peripheral angiospasm without elevation of the systemic blood pressure. The relation of this condition to Buerger's disease (thromboangiitis obliterans) and Raynaud's disease will be discussed later.

A few other tests may produce information of value. The ascorbic acid of the blood is often low, even in persons receiving a normal diet. The basal metabolic rate is low and the cholesterol of the blood high in a few instances, and the amount of noniodizable calcium in the blood may be low. There may be relative achlorhydria, according to Marquardt, although gastric analysis was not done in most of our cases.

Undoubtedly, there are a number of persons with vasoneurotic disturbances who show no pathologic condition of the eyes, and in certain patients with ocular lesions of various types a tendency to peripheral angiospasm may be revealed which has no relation to the ocular condition. My reference to the swinging of the pendulum was prompted chiefly by the work of Duggan.[5] He has emphasized the factor of angiospasm in a variety of conditions, many of which were considered, for what seemed good and sufficient reasons, to be of inflammatory origin. While local vascular spasm may play a part in the edema which accompanies inflammation, Duggan's work seems to have resulted in a certain confusion. Attention has been directed away from a search for the causative factor in these conditions, and the supposed effect of treatment by vasodilators has, it seems to me, been unduly emphasized. In most of his cases the pressor tests previously described were not done, and treatment was empiric.

CENTRAL ANGIOSPASTIC RETINOPATHY

It is the purpose of this communication to describe a few fairly well defined types of pathologic processes involving the eyes, chiefly two, in which peripheral angiospasm seems to be the causative factor, and to urge that patients presenting signs suggestive of these conditions be submitted to an examination which will determine whether or not abnormal peripheral angiospasm is present.

The most important of these conditions is what Marquardt and I[6] called central angiospastic retinopathy. In the use of this term we followed Horniker, but we preferred the term retinopathy to that of retinitis. The term retinitis seemed to us especially unfortunate, since it is our conviction that the condition is not inflammatory, but is due entirely to a circulatory disturbance.

In our former communication[6] the literature was reviewed, and reasons even were given for identification of this condition with that described by a number of previous authors under various names. These terms included central recurrent retinitis (von Graefe), retinitis centralis (Asayama), retinitis centralis annularis (Kraupa), choroiditis centralis serosa (Riehm), preretinal edema (Guist) and idiopathic flat detachment of the retina (Walsh and Sloan). In most of the reports by these authors, the condition was claimed to be inflammatory, and, as usual, tuberculosis was invoked as the probable cause. This was done by the reporters of a remarkable series of cases in Japan. Matsuoka, for example, collected the records of 640 cases, and Kitahara reported 150 cases in his personal experience. In view of what is now known of the condition, one may add to various more or less scientifically verified impressions of the Japanese the conviction that they certainly must be a spastic little people. A few authors, such as Kraupa and Fuchs, suspected the circulatory origin of the condition, but it remained for Horniker, in 1927

5. Duggan, W.: Am. J. Ophth. **26**:354, 1943.

6. Gifford, S. R., and Marquardt, G.: Central Angiospastic Retinopathy, Arch. Ophth. **21**:211 (Feb.) 1939.

to 1937,[7] to look for other signs of angiospasm and to find them in most of his 42 cases. His methods of examination were not as accurate as those employed at present, but the response of his patients to the use of sedatives and vasodilators must be considered additional evidence that the condition he described was due to spasm of the smaller retinal vessels or, in some cases, of the capillaries themselves.

Early Series.—Our report[6] dealt with 8 patients. In 6 the condition was typical in that only the area of the macula was involved, while in 2 patients some of the larger retinal vessels were also occluded. Special examination of the peripheral vascular system was made in only 6 patients, all of whom showed evidence of angiospasm (table). All 8 patients were males, between 17 and 43 years of age. Nearly all smoked. The typical picture was that of sudden reduction of central vision. This varied from a slight loss, with a small relative central or paracentral scotoma, to a reduction to 20/200. Either one or both eyes were involved, and often there was a history of previous attacks. Metamorphopsia was a common symptom in cases in which there was slight visual loss. During the acute attack the predominant change in the fundus was edema, involving either the whole macular area or some part of it (figure, *A*). With the fine beam of the Friedenwald ophthalmoscope, this area was seen to be distinctly elevated, as shown by bending of the beam. The splitting of the beam described by Walsh and Sloan, which led them to diagnose the condition in their cases as flat detachment of the retina, was not seen, and for a number of reasons it was considered that swelling was present in the retina itself, particularly in the nerve fiber layer. The transient hyperopia observed in several patients suggests an actual elevation of the retina in these persons. A striking feature presented by several patients was a pronounced circular reflex surrounding the macular area, and localization of this reflex with the fine beam seemed to confirm Guist's opinion that it represented an elevation of the internal limiting membrane due to edema fluid. Small hemorrhages were seen at the ends of the visible vessels in only a few patients. The larger retinal vessels were normal in most cases, although constriction of one or more vessels was evident in a few instances and obliteration of several branch arterioles had occurred in 1 case. The occurrence of the edema without involvement of the visible vessels was what led to the conclusion that the capillaries themselves were affected, an opinion shared by Horniker and Bailliart.[8]

Results of Special Examinations in the Reported Cases

Case No.	Average Blood Pressure, Mm.	Oscillometric Data on Ankle: Before Treatment	Oscillometric Data on Ankle: After Treatment	Temperature of Toes: Before Nerve Block	Temperature of Toes: After Nerve Block	Degree of Capillary Spasm *	Acrocyanosis of Toes	Reaction After One Cigaret	Treatment
2	118/80	3.0+	3.0+	32 C. (89.6 F.)	34 C. (93.5 F.)	++++	..	Drop of 4.6 degrees C. (8.2 degrees F.)	Stopped smoking; phenobarbital
4	124/80	2.0	3.0+	28.6 C. (83.4 F.)	32.4 C. (90.3 F.)	++	++	Drop of 4 degrees C. (7.2 degrees F.) in 6 min.	Tissue extract; phenobarbital; thyroid; stopped use of tobacco
5	130/80	1.5	.....	27.4 C. (81.3 F.)	33.2 C. (91.7 F.)	++++	++	Drop of 5 degrees C. (9 degrees F.)	Stopped smoking; phenobarbital
6	120/70	2.0	2.0	33 C. (91.4 F.)	35.2 C. (95.3 F.)	++	+	Drop of 3.2 degrees C. (6.7 degrees F.)	Stopped smoking; phenobarbital; typhoid vaccine intravenously; tissue extract
7	144/90-104/68; low reading after nitrite therapy	1.5	3.0+	25 C. (77 F.)	31.2 C. (88.1 F.)	++++	++	Formerly smoked; drop not measured	Nitrites; tissue extract; typhoid vaccine given intravenously; treated 6 days; stopped smoking
8	128/82	1.0+	3.0+	29.2 C. (84.5 F.)	32.8 C. (91 F.)	++++	++++	Drop of 4.6 degrees C. in 5 min.	Tissue extract; phenobarbital for 6 mo.; stopped smoking

* Observations by capillary microscopy.

In all but 1 of these first 8 patients, restoration of normal vision occurred within two to six weeks, in response to what we called antispasmodic therapy. The edema was replaced in these patients by absorption of fine retinal pigment, which sometimes involved an area larger than the macula (figure, *B*). In some patients fine granular pigment appeared in the macular area; in 1 patient the choroidal vessels became visible, with a line of pigment about the defective area. In a few patients, on whom subsequent reports were furnished by other ophthalmologists, the fundi were said to have returned to normal, but in all patients followed personally signs of absorption of the retinal pigment were observed. In a number of patients, the fine white

7. Horniker, E.: Ann. di ottal. e clin. ocul. **55**:578 and 686, 1927; Arch. f. Ophth. **123**:286, 1929; Klin. Monatsbl. f. Augenh. **98**:487, 1937.

8. Bailliart, P.: Ann. d'ocul. **171**:97, 1934; **175**: 133, 1938.

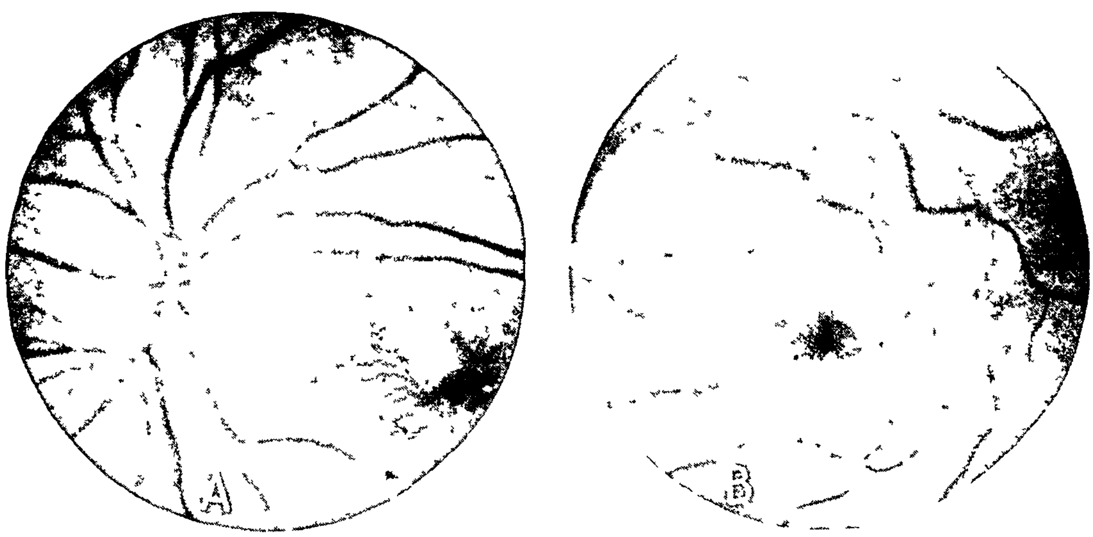
spots, seen by Horniker and Bailliart and erroneously described by them as Gunn dots, were noted.

In none of these 8 patients have recurrences been reported. Most of the patients continued to refrain from smoking, and some continued under moderately intensive antispasmodic therapy for a considerable period. With this therapy most patients gained weight and reported improvement in general health.

Present Series.—Clinical Data: Since the study of this early series, I have seen 23 additional patients with a disturbance which it was felt belonged to this category. Fifteen of these patients were sent to Dr. Marquardt, Dr. Van Dellen, Dr. Mallach or Dr. de Takats for pressor tests. Sixteen were seen during an acute attack, with the typical picture just described. Five were seen only after the edema had subsided; they presented the slight degenerative changes described in this postspastic period. Of these 23 patients, all who were followed showed recovery of normal, or nearly normal, vision. In a few patients vision remained reduced to 20/30 or 20/25, with persistence of a small relative central scotoma. Several patients were seen only once in consultation and were not followed. In 2 patients the changes were more severe and of such character as to cast doubt on the diagnosis or to modify the picture of the condition previously formed. One of these patients, a woman aged 31, presented a typical fundus picture when she was first seen, with the visible vessels normal and extreme macular edema with radiating white deposits, the appearance resembling a macular star. The blood pressure was normal. Vision was reduced to 5/200 and after three months had returned only to 20/100. Some macular edema was still present.

The second patient, a woman aged 30, was observed by Dr. Roy Riser for more than a year. The sharply circumscribed macular edema with a circular reflex was typical, but pictures of the fundus taken during this time showed practically no change in the condition. Vision could be improved by a + 3.00 D. sphere to 20/25, though a relative scotoma was present. The other eye was normal. Pressor tests were not made.

The ages of these 23 patients, with 1 exception, ranged from 25 to 45, with an average of 36 years. The exception was a man aged 21, with normal blood pressure, pronounced pressor reactions, especially to tobacco, and recovery under antispasmodic treatment, with abstinence from tobacco. Whereas in the earlier series only men were affected, of these 23 patients, 8 were women. A number of these women smoked, a few to excess. Their ages ranged from 28 to 40. One showed, in addition to the signs of peripheral angiospasm, evidence of pseudo Addison's disease, with abnormally low systemic blood pressure and a basal metabolic rate of — 20 per cent. In addition to these 23 patients, there were at least 4 in whom spasm of the fine vessels supplying the macula appeared in association with generalized arterial hypertension. Other signs of peripheral angiospasm were present in 2 of these patients, the only ones submitted to the tests, and antispasmodic therapy seemed to be of benefit for the ocular, as well as the systemic, condition, although restoration of function was never so complete as in the younger patients, without systemic hypertension.



A, acute stage in a case of central angiospastic retinopathy; *B,* healed stage.

Owing to the absence of Dr. Marquardt and Dr. Van Dellen on military duty, and the fact that the examinations were conducted in several offices and hospitals, it is impossible to prepare

a table of vascular data including all the points covered in the first report, and in some cases the data seem incomplete. Of the 15 patients referred for special examination, however, all but 2 showed some evidence of abnormal peripheral angiospasm. One of these, a man, had a small healed lesion resembling the lesions developing later in this condition. He showed no signs of retinal edema during observation. The other, a man of 42, gave negative reactions in the pressor tests but had a history of great discomfort on exposure to cold and presented a basal metabolic rate of —22 per cent. He did not smoke. His condition cleared completely on administration of thyroid and injections of tissue extract. Recheck during antispasmodic therapy in a number of cases showed improvement in the degree of angiospasm, the results in some instances approaching normal. It is recognized, however, that the tendency to peripheral angiospasm in most patients a hereditary constitutional anomaly and that measures to prevent or minimize spasm, especially protection against cold and abstinence from tobacco, will always be indicated for these susceptible persons.

Treatment: The treatment employed for most of these patients, in whole or in part, was as follows:

1. Complete abstinence from tobacco was advised, and the body was protected against cold.

2. In the acute stage intravenous injections of papaverine hydrochloride, ½ grain (0.032 Gm.) twice daily, were given for several days, followed by oral administration of ½ grain of the drug three times a day for one to two weeks.

3. In some cases intravenous injections of typhoid vaccine were employed for the vasodilating effect. Small doses, of 10,000,000 to 20,000,000 organisms, seemed as effective for this purpose as larger doses.

4. Use of a hypnotic, either combined with a diuretic in the form of a preparation of theobromine and phenobarbital sodium (theominal), 1 tablet (5 grains [0.325 Gm.] of theobromine and ½ grain of phenobarbital sodium) three times a day, or as phenobarbital, ½ grain three times a day, was continued for several months.

5. Tissue extract, usually an insulin-free pancreatic extract (depropanex), was injected intramuscularly, in a dose of 1 cc. twice a week for fourteen injections, the course being repeated in several cases.

6. The nitrites, including injection of a 10 per cent solution of sodium nitrite by vein, as advised by Duggan, were employed in some cases, but according to Marquardt, the effect of these substances on the small vessels or capillaries is neither as marked nor as prolonged as that of papaverine and the barbiturates, especially a combination of the two.

7. The parasympathomimetic drug neostigmine bromide, in doses of 7.5 to 15 mg. by mouth three times a day, had apparently a good effect.

8. Nicotinic acid was given, either as vitamin B complex or in pure form, in a dose of 150 mg. a day. Its effect on the capillaries was especially notable.

9. A diet containing calcium and the essential vitamins was advised, supplemented when indicated by concentrates of vitamin C and vitamin B complex.

10. Five patients whose basal metabolic rate was lowered received thyroid, and a few women with menstrual disturbance were given an estrogen.

11. A regimen including plenty of rest and avoidance of fatigue and nervous strain was advised when it seemed practical.

12. Checks were made by means of the pressor tests on a number of patients as an indication of the need for further treatment. Patients were advised against resumption of smoking at any time, and use of small doses of barbiturates was continued for some time or was resumed when signs of nervous tension or insomnia developed.

Comment.—Only a few reports on this condition have come to my attention since our early report. Duggan [9] seems to have observed 6 cases of the typical condition previously described, acute attacks responding to the use of vasodilators. He included as instances of a chronic form of the disease 3 cases which seem to me doubtful and 4 cases which he admitted fell in the category of disciform degeneration of the macula. This seems to confuse the issue, and few ophthalmologists would agree with Duggan's statement that "disciform degeneration differs only in degree from the mild lesions of choroidosis seen in young adults." His preference for the name "choroidosis centralis serosa" rests on certain debatable points, which need not be discussed here. No pressor tests were recorded in his brief case report, a positive response to the nitrites evidently being considered sufficient to confirm the diagnosis of angiospasm. Schaub [10] reported 1 case in which the fundic picture seemed typical but recovery

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9. Duggan, W. F.: Choroidosis Centralis Serosa: Diagnosis, Pathologic Physiology and Therapy, Arch. Ophth. **27**:123 (Jan.) 1942.

10. Schaub, C. F.: Am. J. Ophth. **24**:1312, 1941.

was extremely slow. Löwenstein[11] reported 3 cases and suggested that allergy was a probable factor in certain cases. Smitmans[12] observed 9 cases in one year of a condition which he diagnosed as central serous choroiditis. In all cases normal vision was recovered after treatment with calcium, vitamins and papaverine. The earlier literature was reviewed in our previous report.[6]

PERIPHLEBITIS OF THE RETINA

Next to central angiospastic retinopathy, the ocular condition in which the question of retinal angiospasm seems to be of most interest is periphlebitis retinae with recurring hemorrhages in the vitreous. Marchesani,[13] in 1934, first suggested that patients with periphlebitis, a condition usually considered due to tuberculosis, might have a disease of the retinal vessels comparable to Buerger's disease of the extremities, and this theory seemed to be confirmed by examination of the peripheral circulation in his cases. He reported 25 cases, in 3 of which gangrene of the extremities required amputation, while in most of the cases only signs of "latent" thromboangiitis of the extremities were present, as revealed by examination of the extremities and capillary microscopy. In 7 of his cases, in which examination was made by Stander, there was evidence of involvement of the cerebral vessels, including oculomotor paralysis. In 1 of his cases sections of one eye showed thromboangiitis obliterans of the retinal and uveal vessels and no evidence of tuberculosis. Closure of retinal vessels has been described by Lisch[14] and Uyama[15] in cases of Buerger's disease. Lisch,[16] however, in a later study of 35 cases of various forms of peripheral vascular disease, including Buerger's and Raynaud's disease, did not observe periphlebitis. Schmidt[17] observed no signs of peripheral angiospasm in 8 cases of periphlebitis, in all of which there was evidence of tuberculosis.

In view of this somewhat uncertain status of the subject, it seemed of interest to report the observations on a series of patients with such a condition who had been seen since 1939. Of 12 such patients, 7 were referred for examination of the peripheral vascular system. No patient with hypertension, nephritis or diabetes was included, or any in whom trauma was a factor. Patients showing evidence of past or present iritis or choroiditis were also excluded.

The patients were selected on the basis of evidence of severe vascular disease of the retina of the type usually called periphlebitis, with, in nearly all, spontaneous hemorrhages into the vitreous and a tendency to the formation of preretinal bands of connective tissue. Most of the patients were young adults, the average age being 28.6 years at the onset of ocular symptoms. The oldest patient was 42 and the youngest 8 years of age. Eight patients were males and 4 females. In 7 patients more or less satisfactory evidence of tuberculosis was found, consisting chiefly of positive reactions to high dilutions of tuberculin given intradermally and, in some, positive signs in the chest. Their cases will not be discussed further, except for those of 2 who showed evidence of peripheral vascular disease as well. One patient presented no evidence of tuberculosis and was seen before pressor tests were advised. Several foci of infection were removed, and he has been free of recurrences for seven years. Five of the 7 patients referred for examination of the peripheral vascular system showed evidence of peripheral angiospasm, and in 3 of these it was the only factor which could be considered of etiologic importance. Two showed no evidence of angiospasm. One was tuberculin positive, while no etiologic factor could be discovered for the other.

The cases of the 2 patients showing evidence both of tuberculosis and of peripheral angiospasm may be discussed briefly.

A woman aged 25 gave a positive reaction to tuberculin; her basal metabolic rate was —26 per cent, and the cholesterol content of the blood, 187 mg. per hundred cubic centimeters; the pressor tests gave positive results, including a drop of 7.2 degrees (F.) in the temperature of the extremities after smoking. Her condition cleared up on treatment with thyroid and injections of foreign protein, without any tuberculin, and she has remained free of recurrences since she moved to a warmer climate. The changes were early in her case, permitting restoration of 20/15 vision in the only eye affected. It seems at least possible that the vascular condition was of importance in this case.

A man of 43 presented typical periphlebitis retinae, with perivascular sheathing, closure of a number of retinal veins and preretinal hemorrhages, which had organized and showed an ingrowth of new vessels. The reactions to tuberculin were positive, but after a long course of tuberculin therapy, when the reaction was negative, fresh areas of periphlebitis continued to develop. He was referred to Dr. de Takats, who found evidence in the extremities of Buerger's disease. There were absence of pulsation in one dorsalis pedis artery

11. Löwenstein, A.: Brit. J. Ophth. **25**:369, 1941.
12. Smitmans: Klin. Monatsbl. f. Augenh. **105**:733, 1940.
13. Marchesani, O.: Klin. Monatsbl. f. Augenh. **93**: 214, 1934. Marchesani, O., and Stauder, K. H.: Arch. f. Augenh. **109**:281, 1935. Marchesani, O.: ibid. **109**: 124, 1935.
14. Lisch, K.: Klin. Monatsbl. f. Augenh. **99**:812, 1937.
15. Uyama, Y.: Arch. f. Ophth. **137**:438, 1937.
16. Lisch, K.: Klin. Monatsbl. f. Augenh. **102**:228, 1939.
17. Schmidt, R.: Arch f. Ophth. **142**:1, 1940.

and other circulatory changes. A heparin clearance test gave a flat curve of the type seen in the active stage of Buerger's disease. The patient stopped smoking, was given injections of sodium tetrathionate and later was kept under treatment with small doses of dicoumarin (3-3'-methylene bis [4-hydroxycoumarin]) given by mouth. There have been no fresh hemorrhages for some time, and central vision has returned to normal.

The cases of the 3 patients in whom the vascular condition seemed the only cause of the condition deserve a more detailed report.

A woman of 23 presented the picture of unilateral Eales' disease of several years' standing, with recent hemorrhages. The reactions to tuberculin were negative, as were the results of other examinations, except for the pressor tests, which revealed pronounced angiospasm. The patient was treated with barbiturates and tissue extract and had no other hemorrhages during observation. Vision, which was reduced to light perception, showed no improvement, but the other eye remained normal.

M. D., who was seen at the age of 12 years, presented retinal hemorrhages and bands of organizing connective tissue along the vessels about the disks. No evidence of tuberculosis or other infection was revealed, but pressor tests showed pronounced angiospasm, with a drop in temperature of 13 degrees (F.) following the nicotine test. Hemorrhages continued to occur for a time in spite of antispasmodic therapy, and it became impossible to see either fundus. These hemorrhages have finally ceased, and vision in one eye, after removal of the lens, which had become cataractous, is now 20/200. In the other eye a cataract has developed, and projection is faulty.

J. L., a boy of 8 years, was first seen when repeated hemorrhages had reduced his visual acuity to perception of light in the right eye and 6/200 in the left eye. He showed pronounced signs of peripheral angiospasm. The temperature of the toes was low and rose 10.5 (F.) degrees after nerve block. Oscillometric readings were low. Other examinations, including tuberculin tests, gave negative results. On treatment with neostigmine bromide, 7.5 mg. three times a day, he remained free from further hemorrhages for a year, with decided improvement in vision. One hemorrhage occurred at this time, but after treatment was resumed, vision continued to improve and at the end of two years was 20/200 in the right eye and 20/65 in the left eye.

A survey of the material shows that the situation is by no means as simple as that in central angiospastic retinopathy. It must be admitted that in periphlebitis retinae several factors may be responsible and that it is by no means easy to determine from the clinical picture which of these is the most likely one. In some cases, and perhaps in the majority, tuberculosis must be considered of causative importance. In other cases it must be said that no cause can be found. In a small group of cases, however, the factor of peripheral vascular disease seems to be of primary importance. Even in these cases the relation of spasm to the changes in the fundus it produces is by no means as definite as it is in central angiospastic retinopathy. It must be assumed that, as in Buerger's disease, chronic or repeated angiospasm produces organic changes, including, in addition to ischemia of the tissues supplied, stasis in the veins, with perivascular exudation and all the subsequent changes which one sees in the extremities. In fact, for this limited group of cases, the term thromboangiitis obliterans, employed by Marchesani, seems appropriate. Aside from spasm, there may be, as in the case previously mentioned, anomalies in the clotting mechanism, as shown by the heparin clearance and other tests. While the results of treatment are by no means so favorable as with central angiospastic retinopathy, the complete resistance of this much more serious condition to all forms of therapy in the past gives such results as have been reported in these few cases a certain interest.

It would seem that with such a serious condition, obviously involving the retinal vessels, examination of the peripheral vascular system should be included in the complete examination of every patient. Patients showing positive evidence of peripheral angiospasm, even when tuberculin reactions are also positive, may well be given the benefit of treatment designed to improve the peripheral circulation.

ARTERIOLAR SPASM OF THE RETINA

There are other ocular conditions in which peripheral angiospasm undoubtedly plays a part. Some of these, including spasm of the central retinal artery, have been discussed in the previous report. There is space here to speak of only one other condition, illustrated by a single case.

Mrs. K., a woman aged 53, was operated on for senile cataract of the left eye in December 1941. The usual preliminary tests revealed a normal status. After an uneventful intracapsular extraction, vision of 20/20 was obtained. After six months, however, vision began to fail, with no changes in the fundus except gradually progressive diminution in the size of the retinal arterioles. After two months of treatment with thiamine hydrochloride and vitamin B complex in large doses, vision was reduced to 20/80. At this time the patient was hospitalized for examination and treatment by Dr. Van Dellen. He reported a high degree of peripheral angiospasm, and treatment with neostigmine and tissue extract was begun. Vision began to improve slowly, and within four months it was 20/40. The arteries were still rather small. The right eye was operated on at this time, and a vascular condition similar to that in the left eye was revealed, with the best obtainable vision 20/65. Administration of neostigmine bromide was resumed, and two further courses of tissue extract were given. Vision slowly improved in both eyes, and fifteen months after the first operation it was 20/30 in the right eye and 20/20 in the left eye. The vessels of the right eye now showed a definite increase in size, being practically normal, while the disk, which had been pale, had improved slightly in color. The vessels of the left eye were still small, but larger than they had been at the height of the disturbance.

In this case, the only one of its kind in my experience, there seemed to be no doubt that arteriolar spasm was responsible for the loss of vision and that antispasmodic treatment affected the outcome favorably. The difficulty of judging the size of the retinal vessels in cases of aphakia is admitted, but when examination of the fundus reveals no other cause for loss of vision in such cases, or in other cases, and the retinal arterioles appear small, it is logical to advise examination of the peripheral vascular system.

CONCLUSIONS

The records of 23 patients present additional evidence that peripheral angiospasm is the cause of what has been described as central angiospastic retinopathy.

There is evidence that in a certain proportion of young adults with periphlebitis retinae and recurring hemorrhages in the vitreous peripheral vascular disease is the primary cause.

In a case of extreme attenuation of the retinal arterioles with marked peripheral angiospasm following operation for cataract antispasmodic treatment produced improvement.

In all cases in which the characteristics of these three syndromes are presented careful examination of the peripheral vascular system is indicated. In cases of other conditions in which it is desired to employ vasodilators, it would seem logical to advise such an examination before treatment is begun.

Northwestern University Medical School.

DICKEY OPERATION FOR PTOSIS

RESULTS IN TWENTY-ONE PATIENTS AND THIRTY LIDS

FREDERICK C. CORDES, M.D., AND ULRICH FRITSCHI, M.D.
SAN FRANCISCO

In 1935 Dickey conceived the idea of correcting ptosis, in cases with normal function of the superior rectus muscle, by using a sling of fascia lata through the middle third of that muscle and attaching it to the tarsus. This method was published in 1936 as a preliminary report.[1] Although the operation has been in use at the University of California since that time, no further cases were reported until Gifford and Puntenney [2] described their results in 5 cases in which they employed a modification of the Dickey procedure.

Many operations have been devised for ptosis. They may be divided into two principal classes: those employed when there is paralysis or paresis of the superior rectus muscle and those employed when this muscle has normal function. Here we are concerned with the latter.

The Blaskovics [3] operation has been used rather widely. In this procedure a piece of the tarsus is removed and the levator muscle, which has been resected from it, is brought forward and attached to the remaining portion of the tarsus. With complete ptosis this operation has been disappointing.

In 1897 Parinaud [4] and Motais [5] conceived the idea of substituting the middle third of a normally functioning superior rectus muscle for the paretic levator muscle. Since that time the basic principle of the Motais operation has been the one most universally used for correction of ptosis in the presence of a normally functioning superior rectus muscle. Shoemaker [6] modified the operation in 1907 by making an external incision, which gave a better exposure and permitted firmer suturing of the tongue of muscle to the tarsus. Kirby [7] also made minor changes in the operation.

There are several disadvantages to the original Motais operation and its modified forms. The strip of superior rectus muscle sutured to the tarsus may tear out. Even though Kirby [7] advised that it be immediately reattached by a second operation, this complication involves a risk, to be avoided if possible. Another disadvantage is the fact that, since the small strip is attached at one point only, there is a tendency to "tenting" or inverted V formation of the upper lid. The difficulty of performing this operation on small children is such that, in discussing the Motais operation, Bielschowsky [8] stated: ". . . it is not advisable to operate on young children because a child's superior rectus muscle is so small and delicate the suture may easily cut through it." The Motais operation also does not permit an adjustment of the degree of correction to make the lid conform in position to the lid on the other side. The superior rectus muscle is disturbed and injured, and its normal attachment is interfered with. In addition, the dissection entailed is considered difficult. Finally, according to Wheeler,[9] in rare instances, near the attachment of the superior rectus muscle to the upper lid, entropion may occur and the cilia rub on the cornea.

Because of these disadvantages various methods of employing the intact superior rectus muscle have been devised.

From the Division of Ophthalmology, University of California Medical School.

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1. Dickey, C. A.: Superior Rectus Fascia-Lata Sling in the Correction of Ptosis, Am. J. Ophth. **19**:660 (Aug.) 1936.

2. Gifford, S. R., and Puntenney, I.: Modification of the Dickey Operation for Ptosis, Arch. Ophth. **28**: 814 (Nov.) 1942.

3. Blaskovics, L.: Treatment of Ptosis, Arch. Ophth. **1**:672 (June) 1929.

4. Parinaud, H.: New Operative Procedure for Ptosis, Ann. d'ocul. **118**:13 (July) 1897.

5. Motais, E.: Operation for Ptosis by Tarsal Grafting of a Tongue of the Tendon of the Right Superior Muscle, Ann. d'ocul. **118**:6 (July) 1897.

6. Shoemaker, W.: Observations on the Motais Operation for Ptosis, Ann. Ophth. **16**:608, 1907.

7. Kirby, D. B.: Blepharoptosis: The Technique of Its Surgical Correction, Surg., Gynec. & Obst. **70**: 438, 1940.

8. Bielschowsky, A.: Lectures on Motor Anomalies of the Eyes: The Functional Neuroses; Etiology, Prognosis and Treatment of Ocular Paralysis, Arch. Ophth. **13**:751 (May) 1935.

9. Wheeler, J. W.: Correction of Ptosis by Attachment of Strips of Orbicularis Muscle to the Superior Rectus Muscle, Tr. Sect. Ophth., A. M. A., 1938, p. 131.

Wiener,[10] in 1928, advocated the operation suggested by Cannos and Arrangues, in which the levator muscle is severed almost 6 mm. from its tarsal attachment and sutured to the tendon of the superior rectus, so that the tarsus is attached to the latter muscle by means of a portion of the tendon of the levator. As Gifford and Puntenney [2] pointed out, this would "seem to produce an adhesion to the muscle too far from the lid border to accomplish the desired elevation of the lid in cases of complete ptosis."

In 1935 Trainor [11] presented an operation in which a strip of the upper edge of the tarsus is passed under the superior rectus muscle. With simplest operation for ptosis. It does not allow, however, for an adjustment of position of the lid to balance that on the other side. It has the disadvantages pointed out by Spaeth [13] and Gifford and Puntenney [2] that it forms an undesirable adhesion in the upper cul-de-sac which interferes with the movement of the eye and that it buries an epithelial surface (the conjunctiva covering the strip of tarsus) beneath the superior rectus muscle.

In 1938 Wheeler [9] advocated correction of ptosis by attachment of strips of the orbicularis muscle to the superior rectus muscle. Through an external incision the dissection is carried

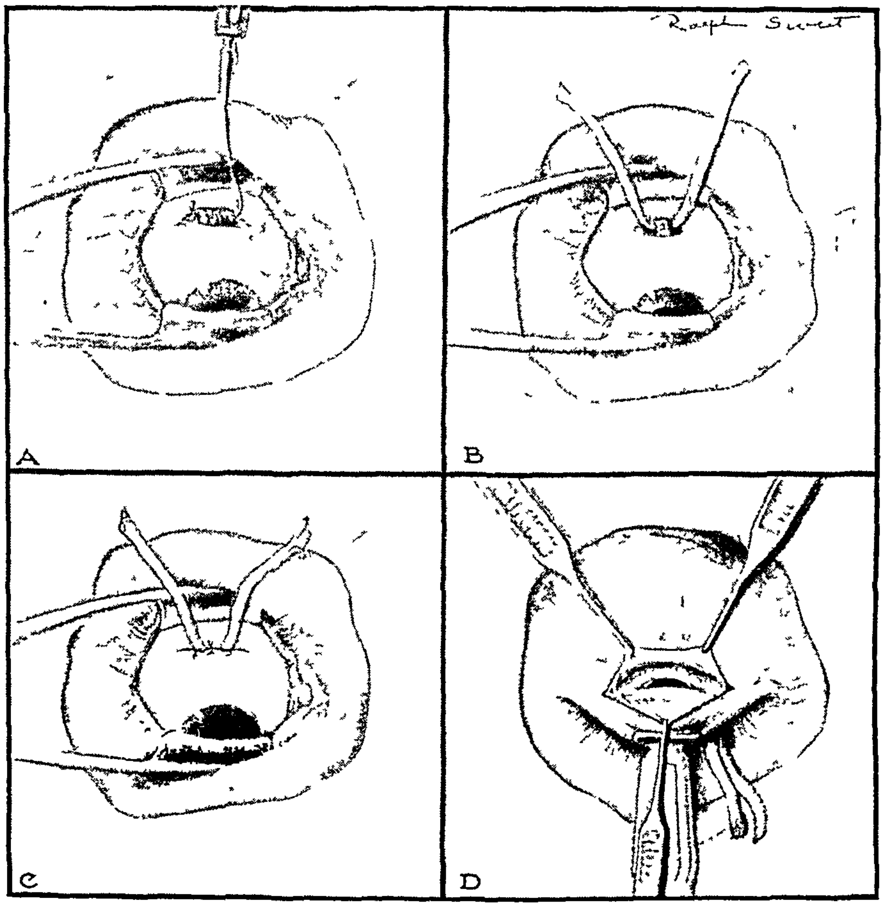

Fig 1.—*A,* isolation of the superior rectus muscle; *B,* insertion of the strip of fascia lata under the central third of the tendon; *C,* conjunctiva and capsule sutured; *D,* tarsus exposed, showing 5 mm incision made through the tendon of the levator muscle at the upper tarsal edge.

the lid everted, an incision is made 2 mm. from the superior edge of the tarsus and parallel with it for a distance of 7 to 10 mm. This strip, with the conjunctiva adherent, is then passed beneath the tendon of the superior rectus muscle and sutured back in place. The procedure has been described and illustrated in detail by Wiener and Alvis.[12] These authors recommended it as the through the orbicularis muscle, the tarso-orbital fascia, the levator muscle and Tenon's capsule, and the superior rectus muscle is picked up on a hook. Strips of orbicularis muscle are then dissected up from the tarsus, and the ends toward the canthi, which have been cut, are attached to the superior rectus muscle with fine catgut. This operation apparently does away with many objections to the Motais procedure, but, as Wheeler

10. Wiener, M.: Correction of Defect Due to Third Nerve Paralysis, Arch. Ophth. **57**:597 (June) 1928.

11. Trainor, M. E.: Operation for Lid Ptosis, Tr. Sect. Ophth., A. M. A., 1935, p. 93.

12. Wiener, M., and Alvis, B.: Surgery of the Eye, Philadelphia, W. B. Saunders Company, 1939, p. 342.

13. Spaeth, E. B.: The Principles and Practice of Ophthalmic Surgery, Philadelphia, Lea & Febiger, 1939, p 368

himself pointed out, the dissection may be considered difficult.

Although there is no perfect substitute for a paralyzed muscle, we feel that the Dickey operation, based on our experience over a period of eight years, has given entirely satisfactory results and that it does away with most of the objections to other procedures. Spaeth,[14] in commenting on the Dickey operation, stated that it undoubtedly provides the firmest attachment any one can obtain between the superior rectus muscle and the tarsus.

incisions are made through the fascia in line of its fibers, about 8 mm. apart, and the fascia is cut between them. This free end of the fascial strip is passed through the loop of the fascial stripper and held taut by a heavy clamp. The stripper is forced down the thigh to the knee, where the fascial strip is cut across by the blade of the stripper. The subcutaneous tissue and the skin are closed in layers by interrupted sutures.

While the fascia is being obtained, an incision is made in the conjunctiva over the superior rectus muscle, and the muscle is exposed and picked up on a hook (fig. 1 *A*). The central third of the muscle is picked up and separated back a short distance. The fascia lata is folded with the muscle surfaces together. This gives it additional strength and also guards against its being cut through by the sutures.

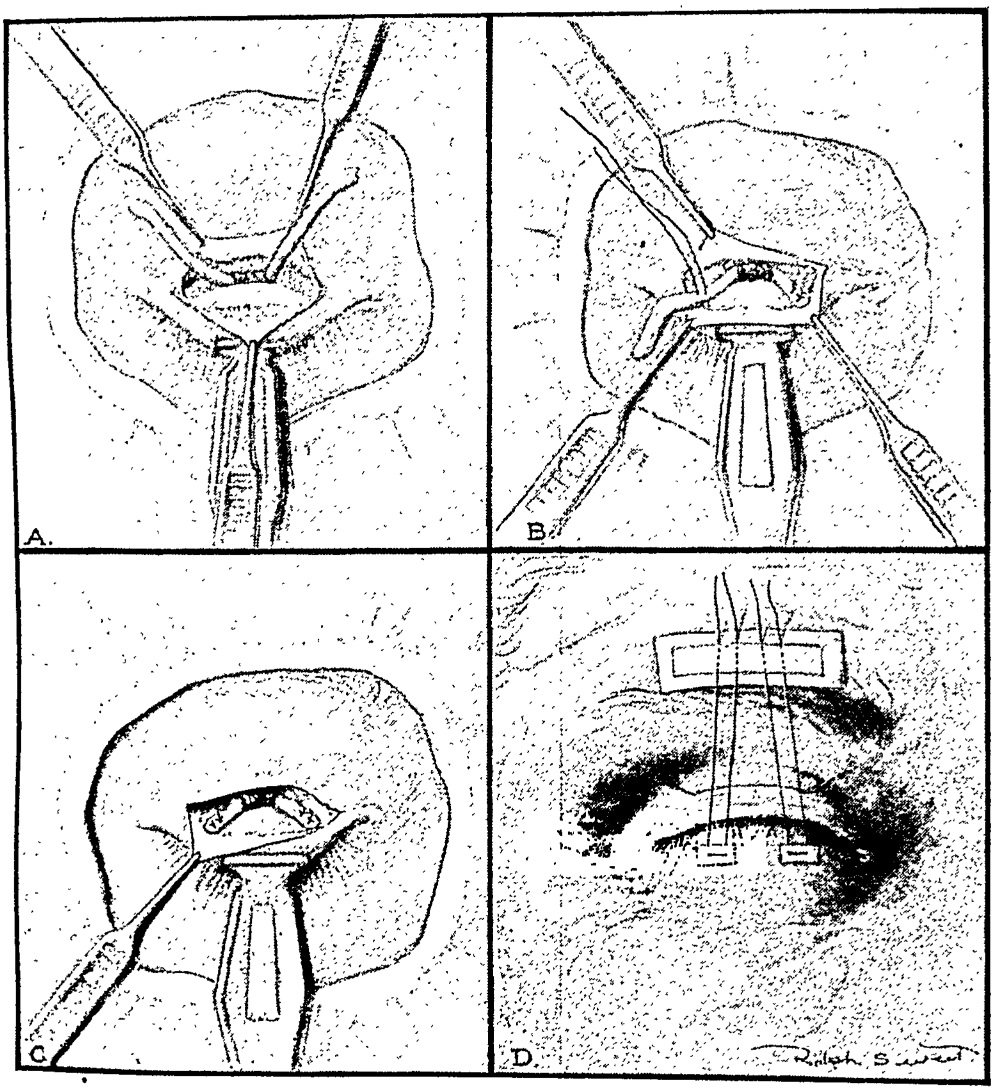

Fig. 2.—*A*, fascia brought through incision in the levator muscle; *B*, sutures through the tarsus and fascia, with the outer sutures tied; *C*, fascia lata sutured to the tarsus; *D*, lid sutures, inserted as advocated by Gifford and Puntenney.[2]

TECHNIC OF THE DICKEY OPERATION

The following technic is utilized: General anesthesia is employed, it having been used in all the cases in the present series. While the preliminary part of the operation is being carried out, a strip of fascia lata 8 to 10 cm. long and 8 mm. wide is obtained by a general or a plastic surgeon. To obtain the fascia a 2 cm. incision is made on the midlateral aspect of the thigh at the junction of the upper and the middle third. This incision is carried down through the subcutaneous tissue until the fascia lata is exposed. The fascia is bluntly separated from the overlying subcutaneous tissue, the stripping being carried toward the knee. Two short parallel

The folded fascia lata is now passed beneath the central third of the muscle (fig. 1 *B*). The conjunctiva and Tenon's capsule over the lateral portions of the muscle are sutured with 0000 catgut. An additional conjunctival suture is placed over the central third of the muscle between the two folded bands of fascia, so that no raw surfaces remain. This does away with the possibility of conjunctival adhesions (fig. 1 *C*). The lid speculum is removed.

A lid clamp with a conjunctival plate (or a Jaeger lid spatula) is introduced under the lid. A horizontal incision, about 20 mm. in length, is made through the skin and the orbicularis muscle 8 mm. from the margin of the lid. The dissection is extended through the orbicularis muscle until the tarsus is exposed well down

14. Spaeth,[13] p. 367.

to the margin of the lid and upward to the upper edge of the tarsus and the tendon of the levator muscle.

At the midpoint of the upper edge of the exposed tarsus an incision 5 mm. in length is made through the tendon of the levator muscle into the conjunctival sac (fig. 1 *D*). The strips of fascia lata are now brought through this opening by forceps and pulled down over the tarsus (fig. 2 *A*).

A double-armed no. 0.009 white silk or linen suture is placed in the tarsus at the junction of the outer and

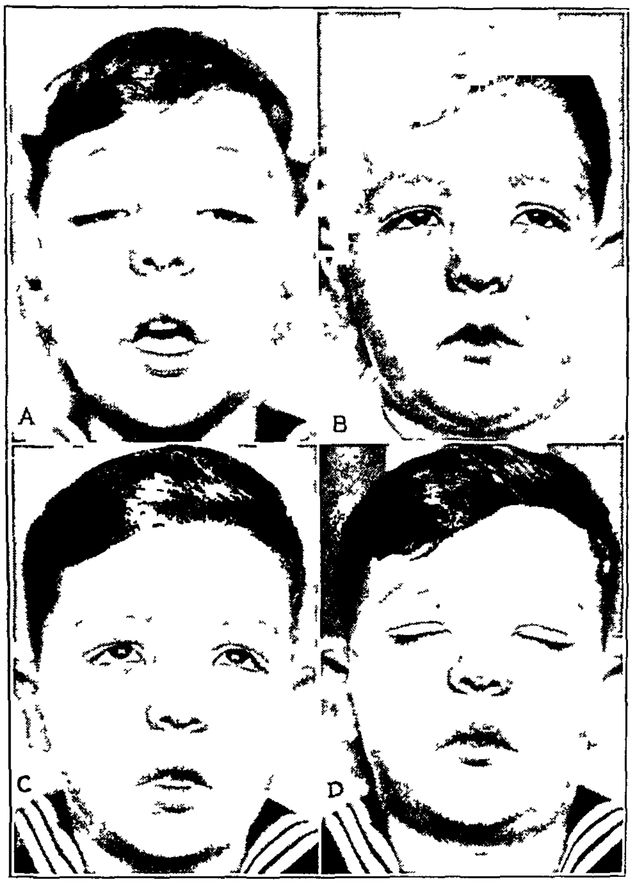

Fig. 3 (case 2).—L. V., aged 4 years, with bilateral congenital ptosis. *A*, appearance before operation; *B*, appearance after operation (note lid folds); *C*, position of lids in elevation, and *D*, lids closed.

the middle third and about 4 mm. from the margin of the lid. Both needles are then passed through the folded fascia and tied firmly, and the suture is cut A second firm bite is taken in the tarsus with another double-armed suture, just below the site of the first suture, and the suture is passed through the fascia lata, tied and cut (fig. 2 *B*). This reenforces the first suture. Another double-armed suture is similarly placed at the junction of the middle and the inner third of the lid and about 4 mm. from the margin (fig. 2 *B*). The lid clamp is removed, and by traction on the fascial loop or sling the site of this suture is determined. The point chosen for this mattress suture will determine the effect obtained and therefore should be carefully estimated. Originally Dickey advised that the point be chosen that will lift the margin of the lid to a point 3 mm below the limbus. More recently we have selected a point 2 mm. from the limbus in most cases, while Gifford and Puntenney found that they obtained satisfactory results with the lid margin 1 mm. from the limbus. The suture is now introduced through the fascia at the chosen point and tied lightly. The position is inspected, and if it is satisfactory, the suture is tied tightly. Another mattress suture is placed just below this suture, introduced through the fascia and tied. The sutures are cut, and the excess fascia lata is trimmed off (fig. 2 *C*).

The position of the lid is now inspected to be certain that the margin is horizontal. If one side of the border is higher than the other, the fascia is adjusted at the point where it passes through the middle third of the superior rectus muscle. In case 19, with partial ptosis, in which the outer half of the lid drooped more than the inner half, the fascia was adjusted to compensate for this difference.

The cutaneous incision is closed with a continuous subcuticular suture, the white fascia sutures being buried. The fibers of the orbicularis muscle fall together of their own accord.

In the past the cornea has been protected by the use of ointment or a moist chamber. We feel that the method employed by Gifford and Puntenney (based on Friedenwald's procedure) is probably better and are now using it. By this method the "protection of the cornea is secured by passing two double-armed sutures through the lower lid and out through the lid border. The sutures are attached to the brow on adhesive tape so

Fig. 4 (case 3).—M. R., aged 2½ years, with bilateral congenital ptosis. *A* and *B*, before operation; *C*, six weeks after operation, and *D*, three years after operation.

as to pull the lower lid up to the new level of the upper lid"[2] (fig. 2 *D*).

The subcuticular suture is removed on the sixth day. The sutures of the lower lid, which may be relaxed by removal of the tape for dressings, renewed every second day, are also taken out on the sixth day.

REPORT OF CASES

The following case reports from the University of California Medical School show the results obtained with the Dickey operation for ptosis. In this series 30 lids, in 21 patients, were operated on by various members of the staff.

CASE 1.—G. C., a boy aged 20 months, was brought to the clinic with the history of bilateral ptosis since birth. The drooping of the lids was so extreme that the patient was compelled to throw his head back in order to see. Operation on the right lid was done on March 11, 1935, and at this time sufficient fascia was obtained for operation on the other side. This fascia was preserved in alcohol and used for the left eye, when it was operated on six weeks later. The result obtained in the right eye was excellent, while the operation on the left eye resulted in complete failure, the fascia, as observed at a second operation, being entirely absorbed. Six months later the left eye was operated on again, without difficulty, and an excellent result was obtained. This was Dickey's first operation, and no attempt has since been made to use preserved fascia.

CASE 2.—L. V., a boy aged 4 years, was brought to the clinic Aug. 19, 1935 because of inability to open his eyes. Except for bilateral congenital ptosis the eyes were normal. On August 26 both lids were operated on, and an excellent result was obtained in both eyes (fig. 3).

CASE 3.—M. R., a boy aged 2½ years, was seen in January 1936 because of bilateral congenital ptosis. On Feb. 4, 1936 both lids were operated on, with an excellent result. A few areas of corneal staining were present for a short time after operation, but these cleared, without corneal scarring (fig. 4).

CASE 4.—D. T., a boy aged 9 years, presented bilateral ptosis, which was almost complete in the left eye. Operation was performed on the right lid on June 9, 1936 and on the left lid on Aug. 13, 1937. A good result was obtained, the position of the lid of each eye being 1 mm. above the upper pupillary border.

CASE 5.—H. L., a woman aged 20, gave a history of progressively increasing ptosis of both lids over a period of five years. The condition had apparently been stationary for the preceding year. After a medical examination, the results of which were essentially without significance, an operation was performed on the left lid on March 23, 1937, with a good result. The patient had vertical diplopia, which persisted until operation was carried out on the right lid, on Oct. 27, 1937. An excellent result was obtained, with good folds in both lids.

CASE 6.—D. T., a boy aged 5 years, presented bilateral congenital ptosis, more pronounced on the right side. Operation was performed on the right lid on June 18, 1937 and on the left lid on Aug. 13, 1937, with excellent results.

CASE 7.—C. H., a boy aged 15, presented congenital ptosis of the left lid, and operation was performed on June 4, 1937. After the surgical procedure there was an overcorrection of about 1 mm. The patient had diplopia on extreme elevation of the lids. He was so well satisfied with the result of operation that he would not consent to further surgical treatment.

CASE 8.—B. L., a man aged 21, had bilateral ptosis and epicanthus, for which operation had been carried out elsewhere two years before the present entrance. A modified Motais operation had been done on both sides. The patient stated that his condition was worse after the surgical procedure. In spite of slight weakness of the left superior rectus muscle, it was decided to perform a bilateral Dickey operation, which was carried out on June 15, 1938. At the time of operation scar tissue was present over the superior rectus muscle, and the tongue used in the Motais procedure appeared to have retracted. Little difficulty was encountered during the operation, and the patient obtained an excellent cosmetic result. He had occasional diplopia during the year and a half that he was under observation. This, however, was not troublesome enough to lead him to consent to further surgical intervention.

Fig. 5 (case 15).—N. G., aged 23, with congenital ptosis; internal strabismus of the left eye, with a 25 degree arc; some weakness of the left superior rectus muscle, and amblyopia of the left eye. Two previous operations had been performed for ptosis—probably shortening of the levator muscle and the Motais procedure. *A,* appearance after two previous operations; *B,* appearance after the Dickey operation; *C,* position of the lid in elevation. There was no diplopia, as a result of amblyopia and suppression.

CASE 9.—A. S., a boy aged 9 years, had an operation on Aug. 7, 1937 for bilateral congenital ptosis, with satisfactory results.

CASE 10.—T. R., a boy aged 4 years, had an operation on Sept. 3, 1937 for complete congenital ptosis of the left lid. The result was excellent. A year later the mother stated that the psychologic effect on the child was "amazing."

CASE 11.—S. J., a girl aged 13 months, had congenital ptosis of the right lid, for which operation was

performed on Oct. 28, 1937. The result was entirely satisfactory. This patient is the youngest on whom the operation has been done. No particular difficulties were involved as a result of the small size of the patient.

CASE 12.—B. M. A., a boy aged 16, had congenital ptosis of the right lid. His grandfather had a similar condition. Operation was performed on the right lid on Jan. 31, 1938, with excellent result. Seven months later he returned with a definite gray band extending across the cornea and running through the lower third of the pupil. The lids were sutured together for three weeks, and at the end of this time there was no staining. When the patient was seen six months later, the condition of the eye was quiet, but a fine linear scar ran across the lower third of the pupil.

Fig. 6 (case 19).—C. M., aged 8 years, with partial ptosis of the right lid from birth. *A,* appearance before the Dickey operation on the right eye; *B,* appearance after operation. A slight overcorrection of the inner half emphasizes the necessity of careful adjustment of fascia.

CASE 13.—F. C., a boy aged 9 years, had partial congenital ptosis of the left lid. The margin of the lid lay at the center of the pupil. Operation was performed on Jan. 4, 1938, the lid margin being placed at the same level as that of the fellow eye. The result was excellent. The patient had diplopia on extreme elevation of the lid This was not troublesome but was still present eighteen months later.

CASE 14.—H. G., a boy aged 9 years, had congenital ptosis of the right lid, for which operation was performed on Feb. 20, 1940, with satisfactory results.

CASE 15.—N. G., a woman aged 23, had complete ptosis of the left lid, associated with an internal strabismus of 25 degrees. There was hyperphoria on the right side, together with some weakness of the left superior rectus muscle. The left eye was amblyopic. Before coming to the clinic the patient had had an operation for the strabismus and two operations for the ptosis. As well as could be determined, the first operation for ptosis had been shortening of the superior rectus muscle, with attachment of the levator muscle. The second operation for ptosis was the Motais procedure. Both operations had failed to correct the defect, so that when we first saw her she had complete ptosis of the left lid (fig. 5 *A*). It was decided that a Dickey operation would offer the best cosmetic results, even though there was some weakness of the superior rectus muscle, together with hypophoria. Since the eye was amblyopic there was no fear of diplopia.

This operation was performed on July 2, 1940. Because of the scar tissue from previous operations, the dissection was a little more tedious but not difficult. On April 29, 1941, a second operation for the strabismus was done. Cosmetically the result was extremely satisfactory, particularly in view of the two previous failures. When the eye is in the primary position there are a little hypophoria, a slight drooping of the lid and some fulness at the outer corner (fig. 5 *B*). While the upward motion of the left eye is somewhat limited, owing to the weakness of the superior rectus muscle, the lid follows the eyeball up, so that there is no great cosmetic disfigurement (fig. 5 *C*). The left eye being amblyopic, there has been no diplopia. While the end result is not as perfect as in the cases of uncomplicated ptosis, we feel that in view of the existing circumstances the operation can be called successful.

CASE 16.—D. C., a boy aged 4 years, had bilateral congenital ptosis, for which an operation was performed on both sides. The results were satisfactory, although the left lid was 1 mm. lower than the right, owing to a slight undercorrection.

CASE 17.—T. P., a boy aged 3 years, had complete congenital ptosis on the right side, for which operation was performed on Feb. 7, 1941, with satisfactory results. After operation some difficulty was encountered in trying to prevent the cornea from drying out, and in spite of all efforts a small corneal infiltrate and resultant scar developed.

CASE 18—L. K., a youth aged 17, had bilateral congenital ptosis. Operation was performed on the right side on June 11, 1941 and on the left side on May 1, 1942, with excellent results in both procedures.

CASE 19.—C. M., a boy aged 8 years, had partial ptosis of the right lid, the margin of which crossed the middle of the pupil. In addition, the outer part of the lid was considerably lower than the inner part. Operation was performed on May 26, 1942, particular care being taken to see that the outer and the inner half of the lid were on the same level. The result was excellent, the position of the lid being at the same level as that of the other eye (fig. 6).

Fig. 7 (case 21).—B. F., aged 10 years, with congenital ptosis on the left side. *A,* before Dickey operation; *B,* after the operation.

CASE 20.—F. M., a boy aged 8 years, had either congenital or obstetric ptosis of the right side, for which operation was performed on July 18, 1942, with excellent results.

CASE 21.—B. F., a boy aged 10 years, had congenital ptosis on the left side (fig. 7 *A*). A Dickey operation was done on Aug. 4, 1942, with a satisfactory result, the left lid now being at the same level as the right (fig 7 *B*).

COMMENT

This series presents 21 cases in which the ptosis was corrected by the Dickey operation, which was performed on 30 lids. Of the patients, 18 were males and 3 females.

The youngest patient was a girl of 13 months (case 11). In view of the difficulty of doing a Motais operation on a patient of this age, it is interesting to note that no complications were encountered and that the result was excellent. The oldest patient was a woman of 23 (case 15), whose case warrants special comment.

In this series there was 1 instance of outright failure (case 1), probably due to the fact that preserved fascia was used. In 2 instances (cases 15 and 16) there was slight undercorrection. In case 15, in which the lid had twice been operated on, without success, there was a good deal of scar tissue, which made the dissection a little more difficult; in addition, a fulness of the outer half of the lid tended to emphasize the undercorrection (fig. 5 *B*). In 1 instance (case 7) there was an overcorrection of about 1 mm.

In 3 cases (cases 1, 8 and 15) previous operations for the ptosis had been performed, without success. In 2 instances the Motais procedure had been used. Aside from the slight inconvenience of dissecting through scar tissue, no difficulties were encountered in the second operation in these cases, and good results were obtained in all of them.

In 3 cases corneal involvement followed surgical correction, a small corneal scar resulting in 2 cases. The corneal reaction occurred during the early convalescent period. This proportion of cases seems rather high, and we feel that the use of the two double-armed sutures through the lower lid, which Gifford and Puntenney [2] suggested and which we are now using, will materially reduce the occurrence of this complication.

It is noteworthy that in none of the cases was there any tendency to "tenting," or an inverted V formation of the palpebral fissure. In addition, in almost every case the lid folds had a normal configuration (figs. 3, 4, 6 and 7).

In 4 cases there was diplopia. In case 5 this disappeared after operation on the other eye. In cases 7 and 13 diplopia was evident only on extreme elevation of the lid. This diplopia was not sufficient to be troublesome and annoyed the patient far less than the ptosis. In case 8 slight weakness of the superior rectus muscle, diagnosed before operation, accounted for the diplopia and was not sufficient to be annoying. In case 15 there was also slight weakness of the superior rectus muscle. Amblyopia in that eye, with suppression, prevented diplopia. Case 8 emphasizes the necessity of careful study of the superior rectus muscle and the eye before operation is contemplated.

Slight weakness of the superior rectus muscle is not a contraindication to the Dickey operation if there is amblyopia or suppression. Also, if the paresis is mild and will cause diplopia only on extreme elevation of the eye, the Dickey procedure is preferable to an operation in which the lid is fixed and does not follow the movement of the eyeball. In the Dickey operation the lid is attached by the fascial sling to the tendinous insertion of the muscle, so that the entire superior rectus muscle aids in holding up the lid; consequently, the presence of slight weakness does not materially alter the action of the muscle. In the Motais procedure, in which the effect is produced by only a portion of the muscle, any weakness would be exaggerated.

In a case in which operation was performed elsewhere diplopia was so marked because of paresis of the superior rectus muscle that it became necessary to undo the results of the operation and restore the ptosis. It is noteworthy that such a procedure is simple. The operator reaches into the upper conjunctival sac with a small muscle hook, such as that used in the O'Connor operation and easily picks up the strips of fascia on either side and cuts them with tenotomy scissors, thus restoring the former ptosis.

The fact that obtaining the fascia lata necessitates an additional surgical procedure has brought forth some criticism. Ptosis is such a disfiguring and distressing condition that any aid obtainable in overcoming it seems justifiable. The obtaining of the fascia is not difficult, and the scar on the thigh is a small one. In none of the cases in which the fascia was obtained was any postoperative complication contingent on its removal. In view of the many advantages of the Dickey operation, we do not feel that the objection to the additional surgical procedure required in obtaining the fascia is justified.

Gifford and Puntenney [2] modified the Dickey operation in that they operated entirely through a cutaneous incision and passed the fascial sling under the entire superior rectus muscle. We can see no real disadvantage to these procedures. We have felt that for the average operator there is less difficulty in isolating the superior rectus muscle through the conjunctival incision. After the fascia has been passed through the central third of the muscle, the conjunctiva is closed on either side right up to the fascia. In addition, another suture brings the conjunctiva together between the two bands of fascia (fig. 1 *C*). The conjunctiva is closed with 0000 catgut, so that it is unnecessary to remove sutures. To date, we have not seen adhesions form in the conjunctival

sac, and in a case previously noted cutting of the bands of fascia restored the ptosis. Gifford and Puntenney apparently limited the Dickey operation to cases of complete ptosis. We have used the operation with excellent results in cases of partial ptosis in which an attempt is made to elevate the lid to the level of that of the fellow eye (cases 13 and 19; fig. 6). In these cases, particularly, it is advisable not to destroy what action the levator may have. Consequently, it seems advantageous to make only a small opening through the tendon at the upper tarsal edge through which the bands of fascia can be passed (fig. 1 *D*), rather than to sever the tendon completely by using a cutaneous incision for the entire operation. Thus, in the event of failure of the operation, the partial ptosis would be no worse than it was before operation. In case 8 a Motais operation had been done elsewhere for partial ptosis. As well as could be determined, it was done entirely through a cutaneous incision. The operation was a failure, with the result, the patient stated, that the ptosis was worse than it had been before surgical intervention.

We have felt that putting the fascial sling through the central third of the muscle allows for a little better adjustment, especially in such cases as case 20, in which one side of the lid was lower than the other. It would seem that in cases of this kind there would be less tendency for the fascia to slip than when it passes beneath the entire muscle.

We have also found that placing the border of the lid 3 mm. below the limbus makes the margin a little low; we therefore have been placing it 2 mm. below. The final decision as to where the border of the lid will be placed depends to a certain extent on the position of the lid in the normal eye. It should be emphasized that the position of the normal lid should be carefully studied before operation is attempted.

SUMMARY

The Dickey operation for ptosis has been used at the University of California for eight years. During this time 30 lids have been operated on in 21 patients, with satisfactory results.

The operation can be used with small children, the youngest patient in this series being a 13 month old child.

In only 3 cases was there permanent diplopia; in 2 of these it was present only on extreme elevation of the lid, and in the third, only at times.

Three lids previously operated on by other methods without success were corrected without great difficulty.

In addition to its use in the presence of a normally functioning superior rectus muscle, the operation can be employed to advantage in cases of slight weakness of the superior rectus muscle in which the corresponding eye is amblyopic or suppresses the image. In these cases the cosmetic result is better than when the position of the lid remains fixed, and with amblyopia or suppression there is no fear of troublesome diplopia.

Owing to the two point suspension, there is no tendency to the inverted V formation of the lid, and the folds of skin show the normal conformation.

The operation permits adjustment of the position of the lid to conform with that of the other side.

The operation has been found satisfactory in cases of bilateral complete ptosis, unilateral complete ptosis and partial ptosis when the action of the superior rectus muscle is normal.

384 Post Street.

ROLE OF SARCOIDOSIS AND OF BRUCELLOSIS IN UVEITIS

ALAN C. WOODS, M.D., AND JACK S. GUYTON, M.D.
BALTIMORE

In a previous report on the etiology of uveitis [1] we stated that the importance of sarcoid and of brucellosis could not then be properly evaluated. The significance of these conditions as causes of uveitis was not appreciated until late in this previous study, and search for evidence of these diseases had not been routinely made. The previous study included patients with uveitis admitted to the Wilmer Ophthalmological Institute up to July 1, 1939. A survey of the patients with uveitis admitted from July 1, 1939 to June 30, 1943 revealed that during this period exactly 200 were completely studied, with the idea of establishing the cause of the uveal disease. Included in the general study were searches for any evidence of sarcoidosis or of brucellosis. It is the purpose of this paper to present the results of the etiologic study of these 200 patients and to discuss the general problems of sarcoidosis and brucellosis as related to uveitis.

The routine diagnostic procedures in the study of these patients were as follows: (1) complete ophthalmic examination; (2) taking of the medical history and general physical examination; (3) routine urinalysis and routine studies of the cellular and chemical constituents of the blood; (4) serologic tests for syphilis; (5) quantitative intracutaneous tests for hypersensitivity to tuberculin, (6) roentgenologic examination of the chest; (7) routine search for foci of infection in the nose, throat, accessory nasal sinuses, teeth and genitourinary tract; (8) gonococcus complement fixation tests; (9) agglutination tests for brucellosis, and for some patients complement fixation tests for the organism, and estimation of the opsonocytophagic index, and (10) when sarcoidosis was suspected, biopsy of a lymph gland or cutaneous nodule, estimations of the albumin and globulin contents of the serum and, in many cases, roentgenographic examination of the hands and feet.

The histories of only 27 of the entire series of 200 patients did not contain these minimal data. These were patients with proved syphilis, sarcoidosis, herpes simplex or gonococcic arthritis. For all of these 27 patients the diagnosis was so clear from the examinations made that irrelevant studies were omitted. In addition to the aforementioned minimal diagnostic procedures, special bacteriologic examinations, sensitivity studies and examinations of the spinal fluid were carried out when indicated. Frei tests for lymphogranuloma venereum were made on a number of patients, but in no instance did such tests appear of diagnostic value. Protection tests for Toxoplasma were not made until 1943.

In this study the criteria for an absolute or a presumptive diagnosis of tuberculosis, syphilis, a focus of infection, gonorrhea and miscellaneous diseases as etiologic factors are exactly those outlined and described in our previous paper. The criterion for the diagnosis of sarcoidosis as the etiologic factor is the histologic demonstration of lesions of the disease in an excised gland or a cutaneous nodule. There is no "presumptive" diagnosis of sarcoidosis. The criteria for the diagnosis of infection with Brucella as the etiologic factor are the elimination of other obvious causes for the uveal disease and the presence of a positive serologic reaction or evidence of sensitivity to such an infection. It thus follows that all the diagnoses of brucellosis as the etiologic factor are in a sense presumptive.

One third of the 200 patients were from private practice, and two thirds were from the public wards. No strictly outpatients were included in this series. With only an occasional exception, all the patients were examined and studied under the direction of one of us.

The results of the etiologic study of these 200 patients are shown in table 1.

As in the former study, the patients reported on here are divided into two groups: Group 1 consists of 102 patients for whom the results of the study were so conclusive that an absolute diagnosis appeared justified, and group 2, of 98 patients for whom the accumulated evidence was not conclusive. For 76 of these patients evidence was sufficient to permit a presumptive diagnosis, but for 22 patients the study was either totally

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From the Wilmer Ophthalmological Institute of the Johns Hospkins Hospital and the Johns Hopkins University School of Medicine.

Read at the Forty-Eighth Annual Session of the American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 13, 1943.

1. Guyton, J. S., and Woods, A. C.: Etiology of Uveitis: A Clinical Study of Five Hundred and Sixty-Two Cases, Arch. Ophth. 26:983 (Dec.) 1941.

unproductive or so inconclusive that no deduction could be drawn as to the cause of the uveitis. The etiologic factors for 22 patients are listed as "undetermined." For purposes of comparison, the table giving the results reported in our first paper [1] is reproduced here (table 2).

Analysis of table 1 and a comparison with the results of the former study, shown in table 2, yield interesting observations. The figure for tuberculosis in table 1 is 41 per cent, and in table 2, 49.7 per cent. In our first series (table 2) the cases of all but 3 patients with sarcoidosis were undoubtedly included under tuberculosis. If the patients with sarcoidosis are added to those with tuberculosis, the incidence for the two diseases is 48.5 per cent in the present study, as compared with 50.2 per cent in the former study. The incidence of syphilis in this study, 14 per cent, is slightly higher than that in the first study, but this increase is accounted for by the admittance to the wards of a few patients with known syphilis for hyperpyrexia therapy. The figures for gonorrhea as an etiologic agent are statistically comparable in the two series—6.5 and 4.6 per cent. Rheumatoid arthritis is listed in this series as a separate etiologic factor, rather than being included under "nongranulomatous systemic infections." This is done in order to make special note of what appears to us to be a definite clinical entity, recurrent serous iritis associated with rheumatoid arthritis and, usually, a specific hypersensitivity to certain streptococcus antigens.

One striking difference between the figures now reported (table 1) and those previously given (table 2) lies in the number of patients whose uveitis was attributed to a focus of infection. In this series the ocular condition of only 6 per cent of the total number of patients was attributed to focal infection. Even if the patients whose disease was attributed to brucellosis were included under "foci of infection," the total would be only 13.5 per cent. This is in contrast to a total of 26.1 per cent in our first series. This difference illustrates clearly our growing disbelief in the importance of focal infection as a frequent cause of uveal disease and the unwillingness of our consultants to lay stress on trivial and minor foci of infection which appear clinically unrelated to the ocular condition. Consequently, the incidence of uveitis of undetermined origin is much higher in this series.

TABLE 1.—*Etiologic Factors of Uveitis, Either Definite or Presumptive, in Present Series of Two Hundred Patients*

Etiologic Factor	Group 1: 102 Patients with Definite Evidence of Etiologic Factor		Group 2: 98 Patients with Presumptive Evidence of Etiologic Factor		Total: 200 Patients	
	No. of Patients	Percentage *	No. of Patients	Percentage *	No. of Patients	Percentage
Tuberculosis	39	19.5	43	21.5	82	41.0
Syphilis	24	12.0	4	2.0	28	14.0
Sarcoidosis	15	7.5	0	0.0	15	7.5
Brucellosis	0	0.0	15	7.5	15	7.5
Foci of infection	4	2.0	8	4.0	12	6.0
Rheumatoid arthritis	5	2.5	0	0.0	5	2.5
Gonorrhea	7	3.5	6	3.0	13	6.5
Miscellaneous	8	4.0	0	0.0	8	4.0
Undetermined origin †	0	0.0	22	11.0	22	11.0
	102	51.0	98	49.0	200	100.0

* Percentages are given on the basis of the total series of 200 cases on which this report is based.
† The 22 cases of uveitis of undetermined origin consist of 9 cases of granulomatous uveitis and 13 cases of nongranulomatous uveitis.

TABLE 2.—*Etiologic Factor: Diagnosis, Either Definite or Presumptive, for 562 Patients with Uveitis*

Etiologic Factor	Group 1: 244 Patients with Definite Evidence of Etiologic Factor		Group 2: 318 Patients with Presumptive Evidence of Etiologic Factor		Total: 562 Patients	
	No. of Patients	Percentage	No. of Patients	Percentage	No. of Patients	Percentage
Tuberculosis	132	23.5	147	26.1	279	49.7
Syphilis	45	8.0	14	2.5	59	10.5
Sarcoid	3	0.5	0	0.0	3	0.5
Brucellosis	1	0.2	1	0.2	2	0.4
Foci of infection	31	5.5	116	20.6	147	26.1
Gonorrhea	10	1.8	16	2.8	26	4.6
Nongranulomatous systemic disease	14	2.5	19	3.4	33	5.9
Metabolic disease	0	0 0	3	0.5	3	0.5
Miscellaneous	8	1.4	2	0.4	10	1.8
Total	244	43.4	318	56.5	562	100.0

COMMENT

Sarcoidosis.—The term "sarcoid" was first used in 1899 by the Norwegian dermatologist Boeck,[2] who described the cutaneous manifestations of the disease. The changes he described were later shown to be similar to those described in 1889 by Besnier [3] under the name of "lupus pernio." Boeck later changed his first concept of the relation of these cutaneous changes to sarcoma and termed the condition "benign miliary lupoid." In 1914 the modern concept of this disease was stated by Schaumann,[4] who recognized the disease to be a chronic granulomatous disorder of uncertain course and spotty distribution, relatively benign, capable of affecting any organ in the body but with considerable predilection for the reticuloendothelial system. He termed the disease "benign lymphogranulomatosis." The disease is variously known under these, and other, appellations and is associated with the names of these three authors. The most popular name is the misnomer applied by Boeck—"sarcoid." Within the last few years this disease has received widespread attention, and a number of excellent reviews have appeared, notable among which are the reports of Scott [5] (1938), Harrell [6] (1940) and Longcope [7] (1941).

In general, sarcoidosis is a relatively benign, chronic disease, occasionally punctuated with acute exacerbations. The constitutional symptoms are slight, and while fever may be present in the early stages in some cases, more frequently it is entirely absent. The clinical symptoms produced by sarcoidosis are usually the result of local mechanical obstruction, with consequent irritation and interference with function, rather than of general toxemia or a systemic reaction. A peculiar laboratory observation reported in about 90 per cent of patients with sarcoidosis is a disturbance in the albumin-globulin ratio of the blood serum, due to an elevation of the globulin. There is no leukocytosis, but sometimes moderate eosinophilia is present. The sedimentation rate is usually increased, as is the calcium content of the blood. Patients with sarcoidosis usually, but not always, show a remarkable anergy to tuberculin, often failing to show any reaction to such large doses as 1, or even 10, mg. of old tuberculin injected intracutaneously.

The characteristic pathologic lesions of sarcoidosis are tubercle-like masses of epithelioid cells, usually without any surrounding zone of inflammatory cells, or at best a scanty peripheral sprinkling of lymphocytes (fig. 1). There is

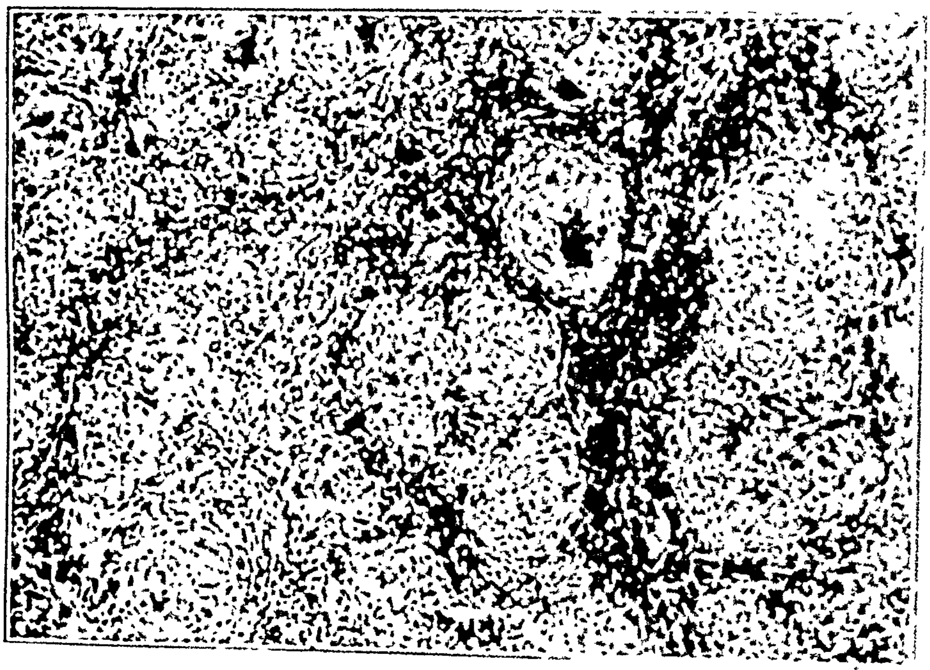

Fig. 1.—Photomicrograph of a lymph node in a case of sarcoidosis.

2. Boeck, C.: Multiple Benign Sarcoid of Skin, J. Cutan. & Genito-Urin. Dis. **17**:543, 1899.

3. Besnier, E.: Lupus pernio de la face: Synovites fongueuses (scrofulotuberculeuses) symetriques des extremites superieures, Ann. de dermat. et syph. **10**:333, 1889.

4. Schaumann, J.: Etude sur le lupus pernio et ses rapports avec les sarcoides et la tuberculose, Ann. de dermat. et syph. **6**:357, 1916-1917.

5. Scott, R. B.: The Sarcoidosis of Boeck, Brit. M. J. **2**:777, 1938.

6. Harrell, G. T.: Generalized Sarcoidosis of Boeck: A Clinical Review of Eleven Cases with Studies of the Blood and the Etiologic Factors, Arch. Int. Med. **65**: 1003 (May) 1940.

7. Longcope, W. T.: Sarcoidosis, or Besnier-Boeck-Schaumann Disease, J. A. M. A. **117**:1321 (Oct. 18) 1941.

rarely any evidence of caseation or necrosis. These tubercles usually, but not always, contain giant cells. In 20 per cent of cases peculiar, hematoxylin-staining, usually doubly refractive inclusions, known as Schaumann bodies, are seen in the giant cells. If Schaumann bodies are not present, it is impossible to differentiate lesions of sarcoidosis histologically from the "hard" tubercles of tuberculosis. In sarcoidosis these individual clusters of cells remain small but usually become numerous, forming macroscopic nodules with a proliferative tendency. They may remain unchanged for months or years, usually healing with scanty fibrosis and hyalinization.

While the nodules of sarcoidosis occur diffusely throughout the body, they have a decided predilection for the reticuloendothelial system. Generalized or spotty glandular enlargement is frequent, and the lymph glands practically always show the characteristic microscopic lesion. Roentgenologically visible lesions of the lungs are present in the majority of cases, principally in the form of diffuse infiltration, more noticeable at the hilus and in the lower portion of the lungs. Nodules of the skin of varying size and consistency occur in about one-half the cases. The liver and spleen are likewise involved in about 50 per cent of cases of this disease. Less frequent, but characteristic, manifestations of the disease are the rarefaction of the phalanges of the hands and feet, peculiar punched-out areas visible on roentgenographic examination. Nerve palsies, especially of the facial nerve, occur in the uveoparotid type of the disease. Lesions of other structures, the heart, muscles or meninges, are not often evident clinically but are frequently observed on microscopic examinations. It should be emphasized that while the lesions may be widespread, the distribution is spotty, and the individual patient usually shows only a few of the various clinical manifestations of the disease.

The cause of sarcoidosis is unknown. The elevation of the serum globulin, the antibody-containing protein of the blood serum, suggests that the disease may be the result of an actual infection, but no infectious agent, either virus or bacterial, has ever been isolated. Because of the similarity of the pathologic lesions to hard tubercles and the fact that about 10 per cent of patients with sarcoidosis later have frank tuberculosis, the relationship of sarcoidosis to tuberculosis has repeatedly been suggested, including the possibility that sarcoidosis may be due to an attenuated human strain of the tubercle bacillus or to some similar mycobacterium, such as the avian strain. However, the characteristic caseation and necrosis of tuberculosis are rarely seen in lesions of sarcoidosis; all experiments on transmission and inoculation have been fruitless, and anergy, rather than hypersensitivity, to tuberculin and various strains of mycobacteria is the general rule.[8] The fact that some patients with sarcoidosis later have tuberculosis is due probably to the widespread involvement of the lungs by sarcoidosis and consequent impairment of function and resistance to tuberculosis.

The presumptive diagnosis of sarcoidosis depends on the demonstration of the clinical manifestations of the disease, the cutaneous changes, the pulmonary infiltration, the rarefactions of the bones of the hands and feet, the elevation of the globulin in the serum, and the frequent anergy to tuberculin. Williams and Nickerson[9] demonstrated that sarcoid material taken for biopsy when injected beneath the skin of patients with sarcoidosis produces typical nodules of the disease. Later investigators demonstrated that any inert material, such as killed staphylococci and pigment granules, would produce the same effect. This reaction is of some diagnostic value in Negro patients. The absolute and final diagnosis of sarcoidosis must depend on the demonstration of characteristic lesions in biopsy material, usually a lymph gland.

The first report of ocular involvement associated with sarcoidosis was made by Schumacher,[10] who observed iritis in a recognized case of sarcoidosis. Within the next decade a sprinkling of such cases was reported. Ophthalmologic interest in sarcoidosis was stimulated by the almost simultaneous reports of Bruins Slot,[11] in 1936; of Longcope and Pierson,[12] in 1937, and of Pautrier,[13] in 1938, all of whom identified sarcoidosis with "uveoparotid fever," a syndrome first described by Heerfordt,[14] in 1909. Prior to

8. Brooke, W. S., and Day, R.: Skin Sensitivity to Mycobacterial Tuberculins in Sarcoidosis, Bull. Johns Hopkins Hosp. **72**:101, 1943.

9. Williams, R. H., and Nickerson, D. A.: Skin Reactions in Sarcoid, Proc. Soc. Exper. Biol. & Med. **33**:403, 1935.

10. Schumacher: Fall von beiderseitiger Iridocyclitis chronica bei Boeckschem multiplem benignen Sarkoid, München. med. Wchnschr. **56**:2664, 1909.

11. Bruins Slot, W. J.: Besnier-Boeck's Disease and Uveoparotid Fever (Heerfordt), Nederl. tijdschr. v. geneesk. **80**:2859, 1936.

12. Longcope, W. T., and Pierson, J. W.: Boeck's Sarcoid (Sarcoidosis), Bull. Johns Hopkins Hosp. **60**: 223, 1937.

13. Pautrier, L. M.: Les lesions oculaires de la maladie de Besnier-Boeck-Schaumann (le syndrome de Heerfordt), Arch. d'opht. **2**:689, 1938.

14. Heerfordt, C. F.: Ueber eine "Febris uveoparotidea subchronica" an der glandula parotis und der Uvea des Auges lokalisiert und haufig mit Paresen cerebrospinaler Nerven kompliziert, Arch. f. Ophth **70**:254, 1909.

the publication of Slot's paper, Hamburger and Schaffer[15] had expressed the view that uveoparotid fever and certain forms of the Mikulicz syndrome associated with uveitis represented the same fundamental condition. Since the publication of the papers by Slot, Longcope and Pierson and Pautrier, it is generally recognized that these conditions are both manifestations of sarcoidosis.

While sarcoidosis may affect the ocular adnexa as small nodules in the conjunctiva, lids, episcleral tissues and orbit, such lesions are of little importance except for the diagnostic problem they present. The important ocular lesions are those affecting the uveal tract. Notable among the many reports on the ocular complications of sarcoidosis are those of Pautrier[13] (1938), Walsh[16] (1939) and Levitt[17] (1941). The most characteristic clinical picture is nodular iritis, quite similar to the nodular iritis of tuberculosis, although the nodules have a tendency to be larger, slightly pinker and more vascularized. The iritis is characteristically quite painless. Again, there may be no macroscopically visible nodules but the inflammatory reaction is pronounced. In either type posterior synechia may form, and the picture may develop into generalized uveitis, with blurring of the media, secondary clouding of the lens, keratitic deposits and changes in the posterior portion of the uvea. In some cases the condition may progress to secondary glaucoma and finally to phthisis bulbi, but the general tendency is more favorable. The nodules tend to become hyalinized; the inflammatory symptoms disappear, and the entire process may subside without residua. Involvement of the posterior part of the uvea without change in the anterior portion is comparatively rare, but several cases have been reported, the ophthalmoscopic picture being that of small spots or larger nodular exudates in the choroid, with slight surrounding inflammatory reaction. Primary infiltration of the cornea does not occur, any corneal clouding being secondary to the disease in the anterior part of the uvea.

In almost 500 cases of sarcoid reviewed by Osterberg[18] only 27 instances of uveitis were mentioned specifically, but apparently the eyes were not examined in all cases, the records of

TABLE 3.—*Summary of Data on Fifteen Patients with Uveitis and Histologically Proved Sarcoid*

Age, Yr.	Race	Sex	Ocular Involvement	Keratitic Precipitates	Nodules in Iris	Enlargement of Lymph Nodes	Serum Albumin, Gm. per 100 Cc.	Serum Globulin, Gm. per 100 Cc.	Evidence in Roentgenogram of Chest	Intracutaneous Tuberculin Reaction, Mg. of O. T.*	Evidence in Roentgenograms of Hands and Feet	Fever	Cutaneous Lesions	Peripheral Neuritis	Comment
13	W	M	Bilateral; generalized	Large	—	Generalized	3.3	2.7	+	—10	—	+	+	—	
15	N	F	Bilateral; generalized	Large	Large	None	3.2	5.1	—	+0.01	—	—	—	+ (VII)	
18	N	M	Unilateral; generalized	Large	Large	Few	4.0	3.3	+	+0.01	—	+	—	—	
19	W	M	Bilateral; generalized	Large	—	Few	5.3	2.3	+	—0.001	ND †	—	—	—	
21	N	M	Unilateral; anterior	Small	—	Few	4.4	3.3	+	—0.1	ND	—	—	—	
25	N	F	Bilateral; generalized	Large	—	Few	3.6	4.8	+	—3	—	—	—	—	Keratitis also
26	N	M	Bilateral; generalized	Large	Large	Few	4.6	3.6	+	+1	ND	—	+	—	
29	W	F	Unilateral; generalized	Large	Large	Few	5.0	2.0	+	—10	—	—	—	—	
30	N	M	Bilateral; posterior	—	—	Generalized	3.9	4.4	—	+0.01	—	+	—	—	Retinal periphlebitis also
30	N	M	Bilateral; anterior	Small	—	Generalized	ND	ND	ND	ND	ND	—	—	—	Enlarged lacrimal glands
31	W	F	Bilateral; generalized	Large	Large	Few	ND	ND	—	—1	—	—	—	—	
33	N	F	Bilateral; anterior	Large	—	None	3.0	4.6	+	+1	ND	+	+	+ (X and XII)	
47	W	M	Bilateral; generalized	Large	Large	Few	ND	ND	+	+10	—	—	—	—	
53	W	F	Bilateral; anterior	Large	Large	None	4.6	2.3	+	—0.1	—	—	—	—	
67	W	M	Bilateral; generalized	Large	—	Few	4.4	2.8	+	+0.1	—	—	—	—	Keratitis also

* Tuberculin reactions if positive (+) are listed as the smallest dose to which the patient was sensitive; if negative (—), as the largest dose with which the patient was tested.

† ND indicates that the examination was not determined or made.

15. Hamburger, L. P., and Schaffer, A. J.: Uveoparotid Fever as a Manifestation of Mikulicz's Syndrome, Am. J. Dis. Child. **36**:434 (Sept.) 1928.

16. Walsh, F. B.: Ocular Importance of Sarcoid: Its Relation to Uveoparotid Fever, Arch. Ophth. **21**:421 (March) 1939.

17. Levitt, J. M.: Boeck's Sarcoid with Ocular Localization: Survey of the Literature and Report of a Case, Arch. Ophth. **26**:358 (Sept.) 1941.

18. Osterberg, G.: Iritis Boeck (Sarkoid of Boeck on Iris), Brit. J. Ophth. **23**:145, 1939.

most of these cases being collected from the dermatologic literature. In contrast, Levitt [17] found that of 100 patients with sarcoidosis whose cases had been reported since 1936, 28 had uveitis and 10 phthisis bulbi. Of 29 patients with proved sarcoidosis studied in the Johns Hopkins Hospital within the past four years, 15, or 52 per cent, had active uveitis. This evidence indicates that ocular involvement is one of the most frequent manifestations of sarcoidosis.

Fig. 2.—Nodules in the iris in a case of sarcoidosis. *A*, early stage, and *B*, late stage.

Previous reports give no indication of the statistical importance of sarcoidosis in patients with uveitis. The incidence of proved sarcoidosis in this series (7.5 per cent) is undoubtedly too high for all forms of uveitis. Only about one third of the general run of patients with uveitis seen at the Wilmer Ophthalmological Institute are admitted for study or treatment. However, during the period covered by this report, practically all patients with uveitis in whom there was any suspicion of sarcoidosis were admitted for clinical study and biopsy. Therefore, the incidence of sarcoidosis among patients with endogenous uveitis as a whole should be about 2 or 3 per cent. The percentage of cases of uveitis associated with sarcoidosis is probably much lower in some sections of this country, because Negroes (common in Baltimore) are much more likely to have sarcoidosis than are white persons.

The 15 patients with sarcoidosis reported in this paper presented no significant sex distribution of the disease, 9 being males and 6 females. There appears, however, to be some predilection of the disease for Negroes, 8 of the patients being Negroes, a ration out of all proportion to the general racial distribution in this region. This is in accord with the incidence in other reports. The ages of our patients ranged from 13 to 67 years. The significant data on the 15 patients are shown in table 3.

The uveitis in the 15 patients with sarcoidosis reported on in this series was bilateral in 12 patients and unilateral in 3 patients. It was always chronic and often severe. The general tendency was for the entire uveal tract to be involved, although the disease was limited to the iris in 3 patients and to the choroid in 1 patient. While the most characteristic symptom of ocular sarcoidosis is nodules in the iris, such lesions were present in only 7 of our patients. The nodules were similar to those described by other authors, being slightly larger, more irregular and somewhat more vascularized than those present in tuberculous iritis (fig. 2). They sometimes disappeared without a trace, in contrast to tuberculous nodules in the iris, which always leave small scars of atrophy where they heal. In the 7 patients with iritis without nodules the picture was clinically indistinguishable from the usual one of chronic granulomatous uveitis. Only 2 of the patients in this series showed deep keratitis and corneal vascularization. Keratitic deposits were observed in all 14 of the patients with anterior involvement. The deposits were usually large, of the mutton fat, epithelioid cell type. In only 2 patients were small lymphocytic deposits observed. In the 1 patient with choroiditis, the lesions were small, poorly outlined and multiple, and there was questionable associated periphlebitis.

The general course of the ocular disease was usually less severe than that of tuberculous uveitis, and several of the eyes healed without any residual damage. However, in several patients involvement of the uveal tract was extreme, and in 1 patient the eye progressed to phthisis bulbi and was enucleated. Histologically, this eye contained a number of moderately large nodules consisting of epithelioid cells and giant

cells (fig. 3). No Schaumann bodies were visible. These nodules were most prominent in the peripheral portions of the iris and in the ciliary body. There were also some diffuse infiltration of lymphocytes in the iris and ciliary body and a few polymorphonuclear leukocytes. The choroid was normal except for small accumulations of lymphocytes. The anterior chamber contained considerable blood, and there were extensive anterior and posterior synechiae. The lens was surrounded by a thin cyclitic membrane.

All 15 of the patients showed systemic manifestations of sarcoidosis. The most frequent lesion was diffuse infiltration of the lungs, this being present in 11 of 14 patients. Glandular enlargement was present in 12 of the patients, but only in 3 was it generalized, being limited in the rest to a few areas, the submental, the cervical, the inguinal or the axillary glands. It is notable that in the 3 patients with no clinical glandular enlargement, biopsy of an apparently normal gland revealed typical lesions of sarcoidosis. Three patients showed only cutaneous lesions, and 2 had peripheral neuritis. Only 4 patients had any fever during the period of observation. In none of the 10 patients who had roentgenograms taken of the hands and feet were any lesions noted in the bones. While it is generally recognized that the distribution of lesions in sarcoidosis is spotty, it is nevertheless interesting that in this group of patients the ocular lesions occurred predominantly in association with pulmonary lesions and glandular enlargement, lesions of the skin and bone being notably few.

Estimations of the albumin and globulin of the serum were made for 13 of the 15 patients; in only 7 patients was the globulin increased more than 3 per cent.

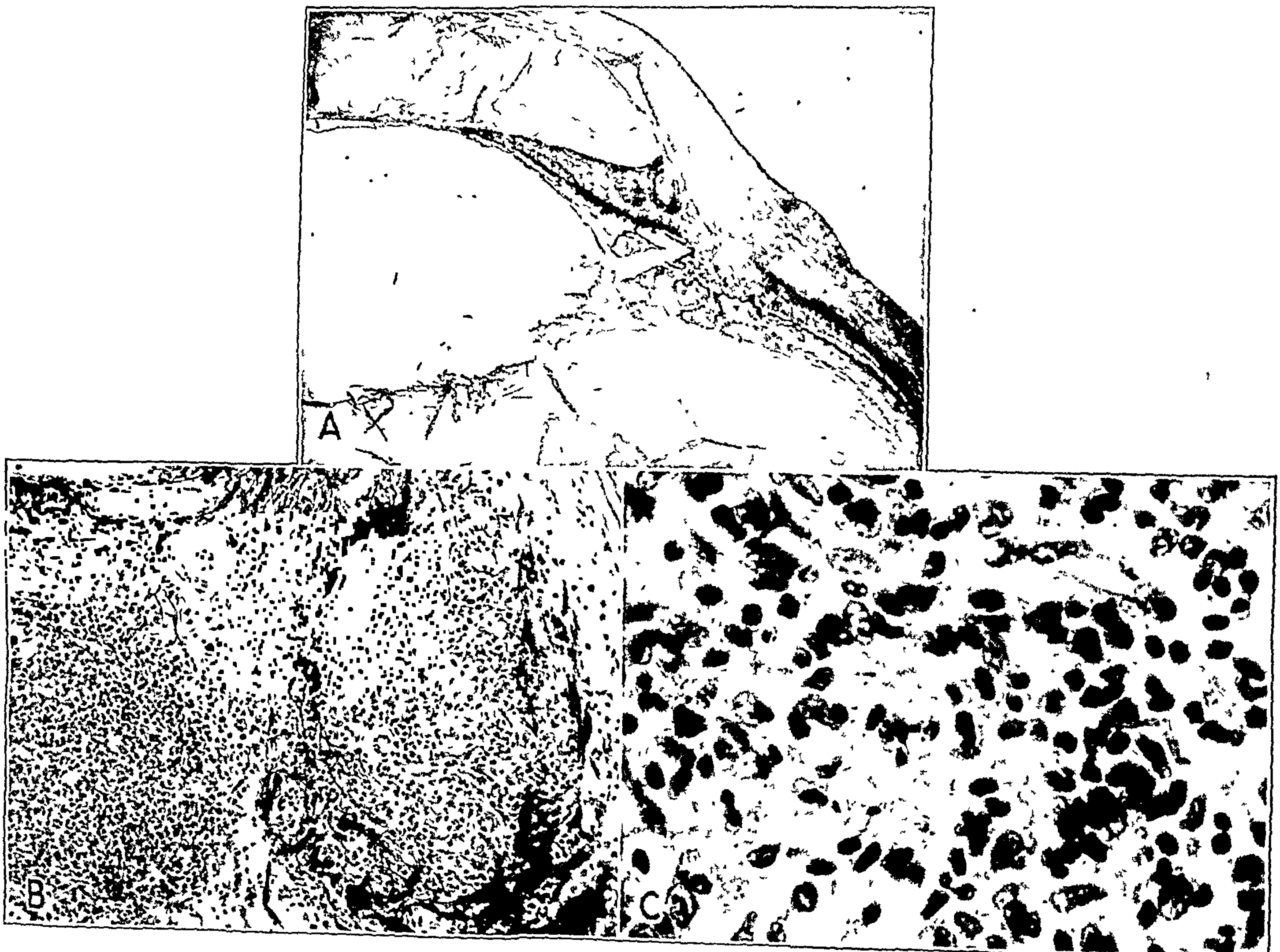

Fig. 3.—Photomicrographs in a case of uveitis accompanying sarcoidosis. *A*, low magnification; *B*, medium magnification, and *C*, high magnification.

Determinations of the sensitivity to tuberculin were made for 14 of these patients. Only 3 patients reacted to 0.01 mg. of old tuberculin, while 5 were completely insensitive to 1 mg. To several of these patients greater amounts of tuberculin were given. Two patients were completely insensitive to the enormous dose of 10 mg., and 1 patient showed only a slight reaction to such a dose.

Brucellosis.—Brucellosis is also known as undulant fever, melitensis, Malta fever and Mediterranean fever. The term brucellosis is derived

from the name of Bruce,[19] who in 1887 isolated the specific organism (Brucella melitensis) from patients with so-called Malta fever. A similar organism (Brucella abortus) was isolated by Bang[20] in 1897 from cows with infectious abortion. In 1913 a third strain (Brucella suis) was isolated from swine.[21] The essential identity of all these organisms was shown by Alice Evans,[22] in 1918, and subsequently the strains of organisms found in animals were shown also to be pathogenic for man.

In man, the disease usually goes through an acute phase, characterized by fever, sweats, malaise, diffuse muscular pains and aches, loss of weight and various more or less vague symptoms affecting any portion of the body. This acute attack may subside without sequelae, but usually the patient passes into a chronic phase, which may last for years. This is characterized by an intermittent low fever, vague pains affecting almost any part of the body and lassitude.

During the acute phase of the disease the specific organisms may be isolated from the blood stream, and a high agglutination titer (up to 1:10,000) is shown by the blood serum. As the disease passes into the chronic stage, the organisms can no longer be cultivated; and the agglutination titer drops, sometimes even falling to zero. A positive complement fixation reaction usually develops against the bacterial antigens of B. melitensis, B. abortus or B. suis. The diagnostic validity of this reaction, however, is somewhat vitiated by the fact that Brucella antigens tend to give false positive reactions or cross reactions with antigonococcus serums. As the patient becomes resistant to the disease, a high opsonocytophagic index may develop. Most irregular of all is a cutaneous sensitivity to brucella organisms, which may develop in cases of the chronic form of the disease. There is no leukocytosis, but often lymphocytosis is present.

The general pathologic changes in acute brucellosis are scanty and are probably limited to chronic passive congestion. In chronic infections in the brucellas there is proliferation of cells of the reticuloendothelial system, especially the spleen and lymph nodes, in the form of small nodules (fig. 4). These tiny nodules often resemble tubercles, with epithelioid cells and sometimes giant cells. At times the nodules have necrotic centers, with polymorphonuclear cells in and around the necrotic zone. Such central necrosis is not regularly noted, but when present it aids in differentiating the lesion from tuberculosis. The heart occasionally shows vegetative endocarditis. Nodular reactions in the meninges are common, and occasionally degenerative changes are seen in nerve cells.

The diagnosis of brucellosis presents considerable difficulty. In the acute stage it is suggested by the clinical picture and by a history of exposure or the ingestion of raw milk or its products. In the chronic stage the diagnosis is suggested by an unexplained intermittent fever, vague general symptoms with pain in the muscles

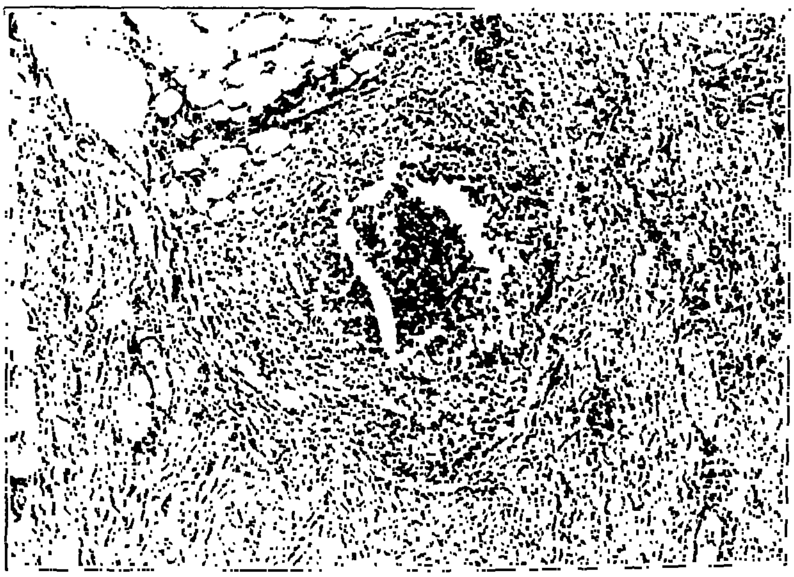

Fig. 4.—Photomicrograph of a lymph node in a case of chronic brucellosis.

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and joints, lassitude and a history of a former, more acute, phase and of the ingestion of raw milk or its products. The only laboratory tests of any value are the serologic and sensitivity reactions. Since in the chronic stage the agglutination titer is usually low, and may even be absent, considerable significance should be attached to weak positive reactions. By use of living organisms in the antigen, weak agglutination reactions may be detected which might be missed with a less sensitive antigen. Positive reactions in complement fixation tests must be controlled by similar tests against gonococcus antigens. A low opsonocytophagic index has no diagnostic significance, and a high index means only that the patient has some resistance against the organisms. All these tests, together

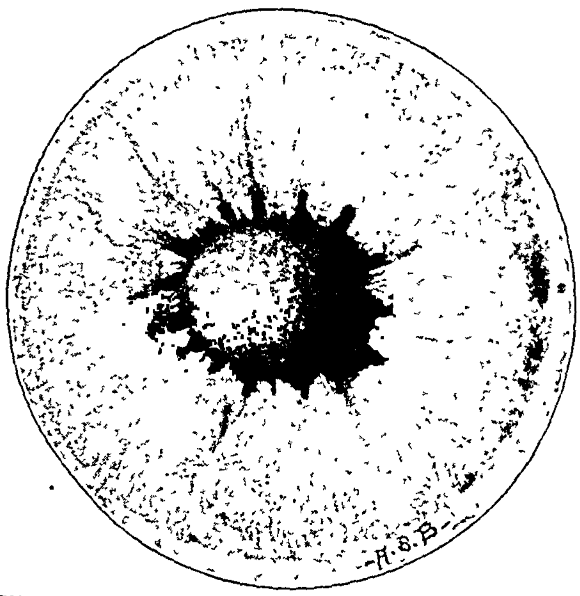

Fig. 5.—Iritis in a case of chronic brucellosis.

with demonstrable cutaneous sensitivity against brucella organisms, only indicate that the patient has had the disease. They do not indicate with certainty that the disease is still active, since a positive reaction may be the residuum of an acute infection from which recovery has been made.

The evidence that systemic infection with the brucella can cause endogenous ocular disease is based on experimental and clinical observations. In 1912 Fabyan[23] reported 3 cases of deep keratitis in infected guinea pigs, lymphocytic infiltration and tubercles in the cornea being observed histologically. Organisms were recovered from the eyes of these animals. In 1928 Orloff,[24] in a comprehensive study of the experimental ocular lesions in guinea pigs, reported that endogenous ocular disease occurred in about 10 per cent of inoculated animals. The affected eyes showed pericorneal congestion; multiple round corneal infiltrates, either central or peripheral, and definite iritis, with exudates over the pupillary space. Histologically, these eyes showed diffuse and focal infiltration of the iris and ciliary body with lymphocytes and epithelioid cells and only minor changes in the choroid. Direct inoculation of organisms in the eyes of rabbits (Burky,[25] 1939) produced generalized keratouveitis almost indistinguishable clinically from severe tuberculous lesions. Interest in ocular brucellosis was stimulated by the presentation of bacteriologic and serologic evidence that most horses with periodic ophthalmia (recurrent endogenous uveitis) are infected with brucellas.

The first clinical observation on ocular brucellosis was reported in 1924 by Lemaire,[26] who studied a case of bilateral optic neuritis in a patient with acute brucellosis, from whose spinal fluid the organisms were isolated. Thereafter, a sprinkling of cases of various types were reported. In 1939 McGinty and Gambrill[27] listed iritis as a recognized complication of brucellosis. In the same year the reported cases were collected by Green,[28] who added 4 of his own. In Green's series were 7 cases of nonrecurrent uveitis in patients with acute brucellosis. The relative infrequency with which uveitis is associated in the acute human brucellosis is indicated by this small number found among hundreds of reported cases of proved brucellosis. Also, Rutherford,[29] in ophthalmoscopic examination of 63 patients with brucellosis, observed changes in the disks in 3, but no uveitis.

The ocular picture in the 15 patients in this series in whom the uveal inflammation was attributed to brucella infection was in no way characteristic or memorable. In 7 of the patients the picture was that of simple recurrent iritis. In 1 patient there were definite nodules in the iris; in another, questionable deep nodules (fig. 5) and in a third, Koeppe nodules. In 3 patients the changes were limited to the choroid, the usual picture being one or more elevated, moderately circumscribed, areas of exudate with little surrounding reaction or generalized subretinal

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edema (fig. 6). In 1 patient there was associated papilledema. In 5 patients the picture was that of generalized uveitis, progressing in 1 to phthisis bulbi. In 12 patients the uveitis was bilateral and in 3 unilateral. In 11 of the 15 patients the uveitis was recurrent. In 8 patients the uveitis appeared to be of the granulomatous type, with thickening of the iris, posterior synechiae and heavy deposits of epithelioid cells on Descemet's membrane. In 7 patients the uveal inflammation was of the nongranulomatous type, without nodular changes in the iris and with only small keratitic deposits of lymphocytes.

In 2 patients there were associated changes in the cornea. In 1 patient these were limited to slight peripheral vascularization, while in the second the picture was that of nummular keratitis. We have also seen typical nummular

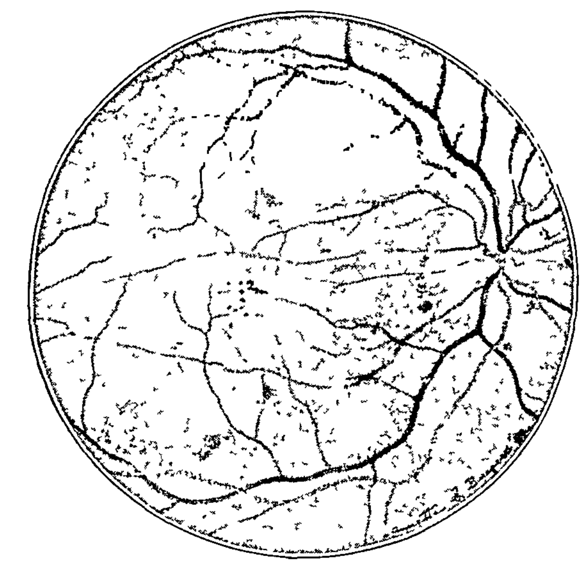

Fig 6.—Choroiditis in a case of chronic brucellosis.

keratitis in another patient with chronic brucellosis. The keratitis was not associated with uveitis and the patient was not included in the present series. These 2 cases, however, suggest the question whether there is any etiologic relation between brucella infection and nummular keratitis. One of the commonest ocular signs associated with experimental brucellosis are corneal infiltrates, similar to those present with nummular keratitis. Further study of cases of nummular keratitis for the possibility of brucella infection is needed for elucidation of this question.

In 1 patient in this series the uveitis had progressed to phthisis bulbi. The eye was painful and was enucleated. Histologic examination showed nonspecific uveitis with several conspicuous lymphoid nodules (fig. 7), a picture suggestive of that of periodic ophthalmia in horses.

None of these patients exhibited any symptoms of acute brucella infection, and only 1 patient had a prolonged, low grade fever. Most of the patients had a history of a previous unexplained fever, with malaise and various vague symptoms. On careful questioning every patient gave the history of ingestion of raw milk or raw milk products, and several had had contact with animals with probable brucella infection. Some of the patients were below par from a general physical standpoint; but others were reasonably healthy, and a few were actually robust.

The clinical diagnosis of brucellosis for these patients was of necessity based almost entirely on serologic and sensitivity reactions as evidence of the infection, although it was bolstered by a suggestive history. Brucellas were not cultured in any case, and, unlike the cases reported by Greene, the disease of all these patients must be considered to be in the chronic, or possibly the healed, stage. Agglutination tests, done against antigens of living B. suis and B. abortus organisms, gave positive reactions in dilutions of 1:40 to 1:320 in 12 of the 15 patients. One patient had an agglutination titer of only 1:20. In another patient the agglutination reaction was negative, but the complement fixation reaction was strongly positive. In the last patient both the agglutination and the complement fixation test gave negative reactions, but the test for cutaneous sensitivity was violently positive, and no other etiologic factors were found. Tests for cutaneous sensitivity were not done routinely, for the reason that they appeared to disturb and to invalidate later agglutination tests. They were made on 5 patients, with a positive reaction in 4 patients and a negative reaction in 1 patient. Complement fixation tests for brucellosis were performed on 8 of these patients, with positive reactions in 6 patients.

Positive serologic or sensitivity reactions are, in the last analysis, only evidences that the patient has at one time in life had a brucella infection, from which he may have recovered, or the disease may have passed into the chronic stage. Moreover, brucellosis is a relatively widespread disease. The question, therefore, arises: What significance should be attached to these positive reactions?

In the entire series, agglutinations against the brucella antigen were performed on 176 patients and gave positive reactions for 22, an incidence of 13 per cent. If the positive reactions are of diagnostic significance, and if brucellosis is an important factor in the causation of uveitis, the percentage incidence of positive agglutination reactions should be higher in a series of patients with uveitis than in a series of "normal" patients,

and should be somewhat comparable to the percentage incidences in medical patients in whom brucellosis was suspected as a factor responsible for their various symptoms. Unfortunately, we have no control series of normal subjects for comparison of positive reactions, but we have a series of 47 medical patients in whom for various reasons chronic brucellosis was suspected and whose serums were sent to the Wilmer Institute for examination. Eight of these patients gave positive reactions, an incidence of 17 per cent. Thus, the incidence of positive agglutination reactions in the entire series of patients with uveitis was almost as high as that in a group of medical patients suspected of having chronic brucellosis. This evidence suggests, but is not statistical proof, that the incidence of brucellosis was higher than normal in the series of patients with uveitis. Of the 22 patients with uveitis with positive agglutinations to brucella, only 8 (36 per cent) had definite evidence of some other factor which appeared to be a cause of the uveitis. Thus, while the incidence of other factors is slightly lower in patients with positive agglutination reactions to Brucella, the difference is not of statistical significance. It is impossible, therefore, from the evidence now available to obtain statistical proof that a positive agglutination reaction to Brucella is of diagnostic significance in establishing the cause of uveitis. Such a positive reaction is, however, suggestive evidence, and in general is probably of about the same value in the diagnosis

Fig. 7.—Photomicrographs in a case of uveitis associated with brucellosis. *A*, lymphoid nodule at the root of the iris; *B*, lymphoid nodule near the sphincter of the iris.

of uveitis due to brucellosis as is moderate hypersensitivity to tuberculin in the diagnosis of tuberculous uveitis.

A total of 76 complement fixation reactions for both the brucella and the gonococcus were performed on patients in this series. Twenty-one patients gave a positive reaction to the brucella, but 18 of these also showed a positive reaction to the gonococcus.

It is clear the diagnosis of chronic brucellosis as the etiologic factor in uveitis must always be presumptive, since the isolation of the actual organism is impossible and there is no therapy so adequate that it can be applied as a therapeutic test. However, despite the presumptive character of the diagnosis, the accumulated evidence indicates that brucellosis is probably an etiologic factor in uveitis, and it may be an important one.

Since a diagnosis of chronic uveitis due to Brucella can never be made with certainty, the incidence shown in this study (7.5 per cent) represents a maximum. The actual incidence of this form of uveitis may be anywhere below this figure.

SUMMARY

A series of 200 patients with endogenous uveitis examined in the Wilmer Institute between July 1, 1939 and July 1, 1943 was subjected to an extensive diagnostic survey, similar to that carried out in a series of 562 patients with uveitis previously reported on. In addition, special tests for sarcoidosis and brucellosis were performed on this series of patients. Such tests were done routinely whenever either of these diseases was suspected. Biopsies of the lymph nodes for diagnosis of sarcoidosis were performed on 51 patients, and determinations of the levels of albumin and globulin in the blood were made on 71 patients. Agglutination tests for Brucella were carried out on 176 patients; complement fixation tests for Brucella, on 76 patients, and determinations of the opsonocytophagic index of the organism, on a number of patients.

In the etiologic classification, a diagnosis of uveitis due to sarcoidosis was made for 15 patients. A histologic diagnosis of sarcoidosis was made for each of these patients. In this group of patients it was noted that the lesions of the skin and bone were notably scarce, that normal levels of globulin in the serum were encountered much more frequently than has been reported for other series of patients with sarcoidosis and that biopsy of a lymph node may yield evidence of this disease even though the lymph gland is not enlarged. Since strictly outpatients were excluded from this series, it is assumed that the uveitis was much more severe than in the usual series of cases and that the actual incidence of sarcoidosis in patients with uveitis examined in the Wilmer Institute is in the neighborhood of 3 per cent.

The uveitis of 15 patients was classified as "probably" due to brucellosis. The diagnosis of chronic brucellosis is difficult, and any diagnosis of uveitis due to infection with Brucella is uncertain. The actual incidence of this form of uveitis is assumed to be less than the 7.5 per cent reported for this series.

Wilmer Ophthalmological Institute.

DEVELOPMENT OF ANTERIOR PERIPHERAL SYNECHIAE IN EXPERIMENTAL ACUTE GLAUCOMA

MANUEL URIBE TRONCOSO, M.D.
NEW YORK

To the memory of my friend, the distinguished ophthalmologist, Dr. John Martin Wheeler.

It has long been debated whether the cause of hypertension associated with acute or subacute congestive glaucoma is exclusively a mechanical one, produced by the application of the root of the iris against the corneal limbus, or whether, on the contrary, the anterior peripheral synechia is the result of preexisting hypertension. Historically, the first position was substantiated by Knies and Weber,[1] who in glaucomatous eyes examined with the microscope always observed an adhesion of the root of the iris to the cornea. However, several observers, including myself,[2] objected that the microscopic sections were made in old glaucomatous eyes enucleated after the process had run its course. On the other hand, microscopic examination of eyes with acute or subacute glaucoma which were removed shortly after the attack, when the patient died of an intercurrent disease (Birnbacher and Czermak [3] and Elschnig [4]), showed that the anterior chamber was totally or partially free from synechiae.

With the advent of gonioscopy the examination of the angle of the anterior chamber could be made directly in living eyes, and I [5] determined for the first time that in cases of prodromal glaucoma or after an acute attack has subsided the angle of the anterior chamber is usually open, either totally or partially. Other authors have confirmed these observations (Werner [6] and Sugar [7]).

Recently, however, the theory of mechanical occlusion of the angle by peripheral synechiae as the principal cause of acute glaucoma has been revived by Sugar [7] and by Kronfeld and Grossman.[8] They based their opinion on the occurrence of the so-called mydriatic glaucoma, which starts immediately or soon after the use of homatropine. Sugar, by gonioscopic examination of such eyes before and after the attack, was able to observe that during hypertension the dilated iris blocked the angle of the anterior chamber. This occurred especially in patients who had shallow chambers, and the root of the iris was near the corneal limbus. By photographic methods, Sugar measured the depth of the anterior chamber in 20 eyes with narrow angles before mydriasis and then instilled homatropine. In 6 of these eyes an attack of acute glaucoma occurred. Sugar and Kronfeld and Grossman concluded that the pathogenesis of the acute attacks is determined, first, by a shallowness of the anterior chamber and, second, by the application of the root of the iris against the trabeculum, which blocks the outflow through the Schlemm canal and upsets the balance of the intraocular pressure. If the upset lasts for several days, the mere contact of the iris to the limbus is transformed into a permanent synechia. Although, of course, in these 6 eyes a mechanical occlusion of the angle may have been the prime factor which started the cycle of hypertension, I do not think this etiologic explanation ought to be extended to include all cases of glaucoma. One should remember that in the other 14 eyes, the majority of which were the fellow, normal eyes of patients with unilateral glaucoma, the mydriatic did not produce any hypertension, al-

This study was aided by a grant from the Harriman Glaucoma Fund.

From the Department of Ophthalmology, Columbia University, and the Ophthalmological Institute of the Presbyterian Hospital.

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though the dilation of the pupil undoubtedly narrowed the entrance to the chamber recess.

As it is difficult to examine the angle of the anterior chamber with the gonioscope during the acute attack on account of the edema and turbidity of the cornea, I have tried to determine experimentally whether the adhesion of the root of the iris is the first step in the production of glaucoma. Unfortunately, there is at present no method of reproducing primary glaucoma experimentally in animals. There have been many attempts to do so by injection of different substances into the anterior chamber or into the vitreous with observations on the variations in tension, the changes produced in the angle of the anterior chamber and the condition of the optic nerve. Injections in the anterior chamber were made, first, with organic substances, such as olive oil (Wever), vitreous (Bajardi), lipids (Weintraub), albumin and serum (Uribe Troncoso) and paraffin emulsion (Ishikawa), and, second, with inorganic substances, such as electrolytic iron (Erdmann, Schreiber and Wengler), dyes (Hamburger) and scarlatoid (Seidel).

Hypertension of a temporary course has been produced by mechanical lesions in the angle (Bentzen), by contusion of the globe (Pesme, Leplat), by cauterization of the limbus with acids (Heirsrath), by irritation of the iris (Magitot) and by discission of the lens (Wessely). Injections in the vitreous have been undertaken with isotonic solution of sodium chloride, by S. Larson; with a solution of sodium oxide, by Redslob, and with histamine, by Duke-Elder and Friedenwald. Ligature of the veins of the vortex (Schulten, Leber, Magitot) produced great venous stasis, with extreme hypertension of a temporary nature.

Unfortunately, the procedures of injection of foreign substances are crude and the results distorted by traumatic and inflammatory conditions. After considering all these methods, I concluded that from the physiologic and pathologic standpoints the best procedure is to use the animal's own serum or blood and to inject it into the anterior chamber or the vitreous. In clinics the production of hypertension, and even permanent glaucoma, is observed after abundant hemorrhages in the anterior chamber. After injuries, and more frequently after operations, such as iridectomy and cataract extractions, an increase in tension develops, sometimes of considerable degree, and may last for weeks or months. It may disappear entirely or leave permanent glaucomatous changes.

The following case illustrates this occurrence.

H. M., an obese woman aged 70, with arthritis, gallbladder disease and systemic hypertension, was admitted to the Ophthalmological Institute for operation for senile cataracts. The tension was 25 mm. in each eye. A preliminary iridectomy was done on the left eye on February 25, and atropine was instilled. There was bleeding from the conjunctiva. The blood entered the anterior chamber, filling it almost completely. After the operation the eye remained tender, and three days later it became painful. The tension rose to 52 mm. Physostigmine did not lower the pressure at first, but on the sixth day the tension fell to 35 and 40 mm., with gradual absorption of the clot in the anterior chamber. Paracentesis of the eye was considered but was not done. On March 6 the hemorrhage in the anterior chamber had partially absorbed. The upper half of the cornea was clear, and the tension was reduced to 35 mm. There was still a great deal of pain and congestion. The tension in the right eye also rose temporarily to 29 mm., but there were no definite symptoms of chronic glaucoma.

On May 22 tension had returned to normal in the left eye. The hypemia was then entirely absorbed, but the anterior chamber remained shallow.

Gonioscopic studies at this time showed that the angle was open on all sides. It was not considered probable that if a peripheral synechia existed at the beginning of hypertension, no traces of it would be evident in this examination.

Intracapsular extraction was performed on this eye by Dr. D. Kirby, on June 9, with complete success. No vitreous was lost. With the proper correction, visual acuity reached 20/40. One year later the patient returned for observation. The results of the operation were still good. Gonioscopic examination at this time showed that the angle had closed on the nasal side but remained open in all other parts of the limbus. This closure was considered the late result of the cicatrization of the incision in the limbus.

Experiments with injections of blood into the anterior chamber had been made previously by several investigators. Riehm [9] observed the effects of these injections in normal rabbit eyes in order to compare them with the changes produced in human eyes affected with tuberculous uveitis; he injected pure blood of the patient into the anterior chamber of 16 rabbits, according to the method of Schieck. In 11 of the animals he obtained hypertension of such high degree that the cornea became opaque and spontaneous rupture of the eyeball occurred in the course of the first two days after the injection. In the other 5 rabbits the hypertension was of less degree, and the absorption of blood took place between one and four weeks after operation. In a second series, of 4 rabbits, he injected defibrinated blood. The effects were milder, and no ruptures of the eyeball were produced. The duration of the reaction was about the same as that in the previous series. Riehm observed, also, that the effect of defibrinated blood became weaker the longer the blood stood after defibrination.

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9. Riehm, W.: Experimentellen zur lokalen Wirkung körper- bzw. arteigenen Blutes in der Vorderkammer des Kaninchens, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **49**:188, 1932.

As these experiments were made from the bacteriologic standpoint, no curves of hypertension were recorded. No microscopic sections were made of the eyes operated on. Riehm ascribed the hypertension produced to an inflammatory reaction, due to "hematogenous uveitis." According to him, the coagulated blood is particularly rich in certain histamine-like substances (adenyl acid or adenosine), which possess a stimulating effect. They are produced by the decomposition of the blood platelets. Freund called them "early" and "late" poisons. The blood is absorbed later by lytic and coagulating injection of defibrinated blood. When the autonomic nerve supply is previously severed, no effect on the vasomotor system occurs.

When I began to study the development of anterior peripheral synechiae and tried to determine experimentally whether the mechanical application of the root of the iris is the first step in the production of hypertension, I considered the several methods of inducing an increase of tension and decided that the best was the injection into the anterior chamber or the vitreous of substances present in the body itself, such as blood serum and pure and defibrinated blood.

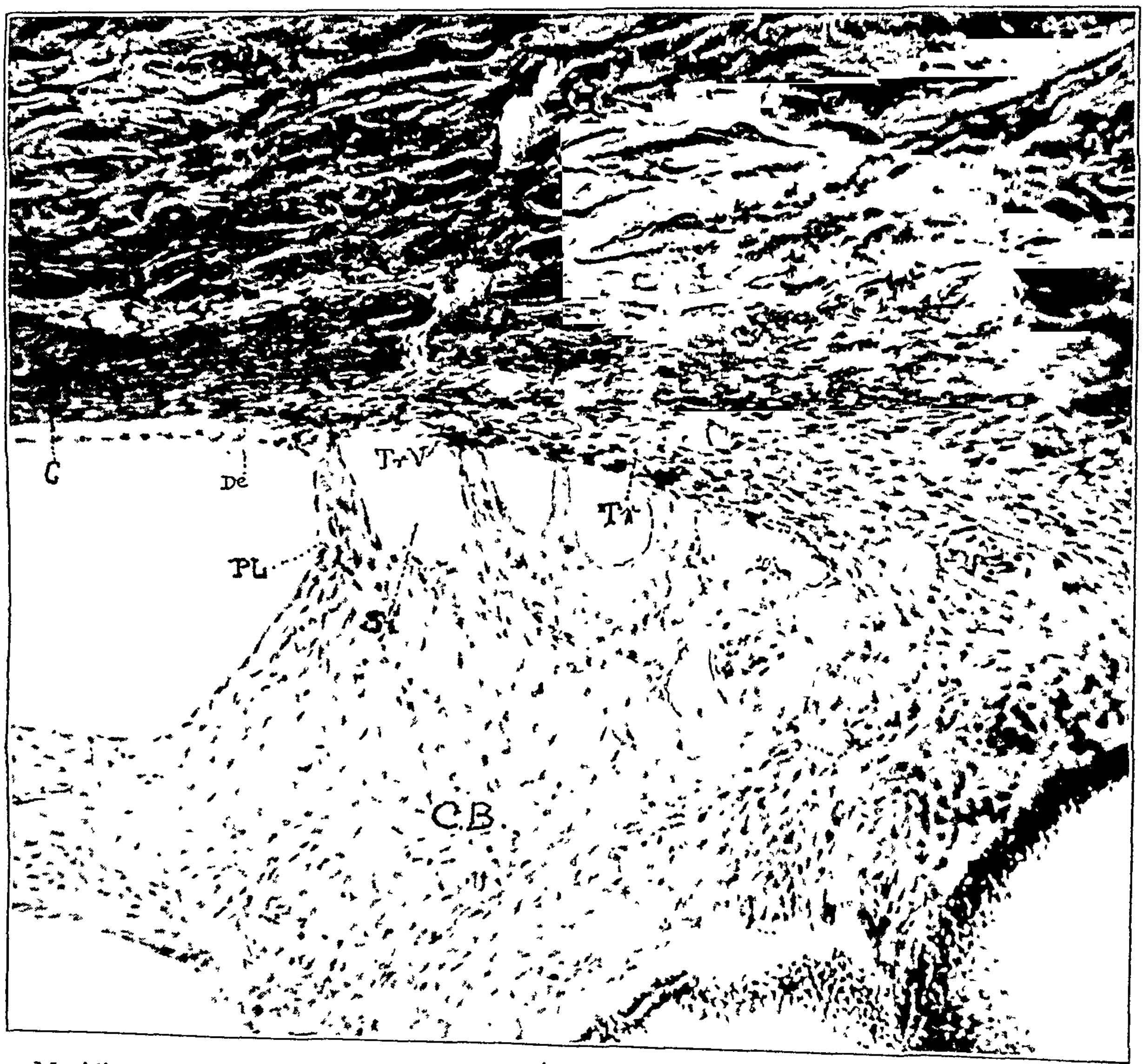

Fig. 1.—Meridional section of a normal rabbit eye (× 45). In this figure, and in the accompanying figures, the following designations are used: *C*, cornea; *D* or *De*, Descemet's membrane; *I*, iris; *PL*, pectinate ligament; *Sc*, sclera; *Si*, ciliioscleral sinus; *Tr.* trabecula; *TV*, trabecular vein, and *CB*, ciliary body.

substances. The general effect of intravenous injection of defibrinated blood has been studied by several authors (Schurer-Waldheim; Hoff; F. Kylin, and Mettenleiter[10]). It immediately produced dilation of blood vessels, combined with reactions of the respective tissues all over the body. These reactions depend on sympathetic and parasympathetic stimulation initiated by the

10. Mettenleiter, M. W.: Autohemotransfusion in Preventing Postoperative Lung Complications, Am. J. Surg. **32**:321, 1936.

The researches described in this paper were conducted only from the physiopathologic standpoint. No effort was made to study changes in the blood in the anterior chamber from the chemical or the bacteriologic point of view.

ANATOMIC CONDITION OF THE ANGLE IN EXPERIMENTAL ANIMALS

The results of animal experimentation cannot be interpreted properly if the observer lacks complete knowledge of the anatomy of the angle

of the anterior chamber and the iris. This omission has led to many errors and encouraged several attempts to consider anatomic and pathologic changes in lower animals as similar to those observed in primates and man. Although the anatomic relations have already been published in other places,[4] a few comments are necessary here for the better understanding of the comparative anatomy of the channels of outflow in the angle of the anterior chamber of rabbits, dogs and monkeys.

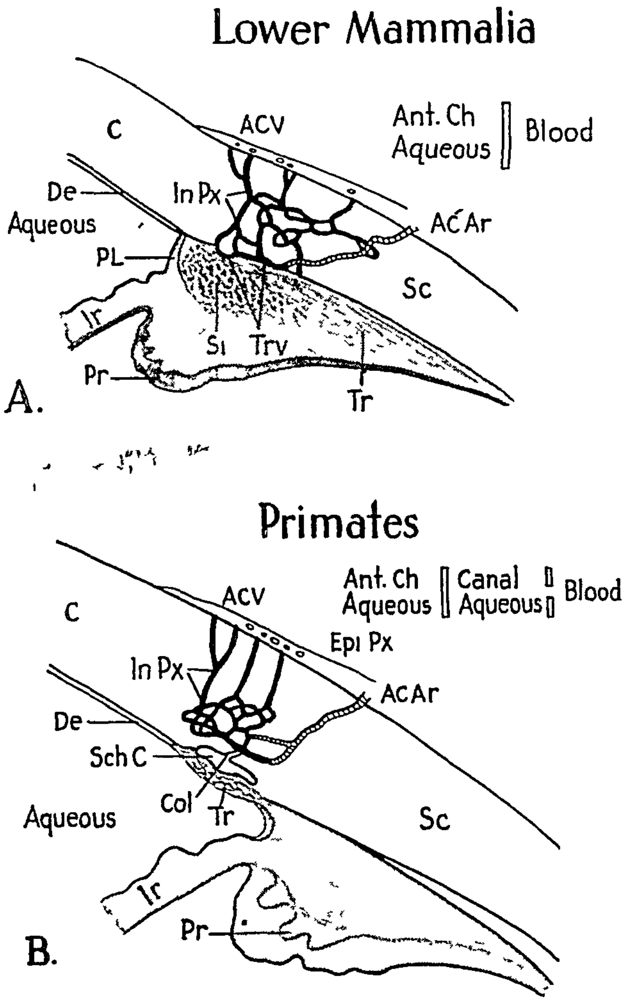

Fig. 2.—*A*, semischematic section of the angle of the anterior chamber in ungulates. Here, and in *B*, *Ir* indicates the iris; *De*, Descemet's membrane; *Si*, cilioscleral sinus, filled with spongy tissue; *In Px*, intrascleral plexus; *Ac Ar*, anterior ciliary artery, and *ACV*, anterior ciliary vein.

B, angle of the anterior chamber in primates. In addition to the designations used in *A*, *Sch c* indicates the canal of Schlemm; *Col*, collector vessel, joined the canal of Schlemm with the intrascleral vascular plexus, and *In Px* and *Epi Px*, the intrascleral and the episcleral plexus

In the rabbit (fig. 1) the anterior chamber terminates at the end of Descemet's membrane exactly at the insertion of the teeth of the pectinate ligament into the sclera. Between these teeth the so-called Fontana spaces communicate posteriorly with a recess of the anterior chamber between the ciliary body and the sclera, which I have called the "cilioscleral sinus." In ungulata the sinus is filled with a meshwork of thin, highly pigmented fibers, resembling a sponge (spongy tissue (fig. 2 *A*, *Si*), while in the carnivora (fig. 6 *P*), instead of this tissue, there are a great number of white, fine meridional strands spread fanlike between the end of Descemet's membrane and the inner, and lower, side of the ciliary body.

Running meridionally at the external wall of the sinus there is in mammals a triangular meshwork structure, with its apex at the end of Descemet's membrane (fig. 2 *A*, *Tr*) which is similar in structure to the trabecula occurring in front of the canal of Schlemm in primates (fig. 2 *B*, *Tr*).

The aqueous coming into the cilioscleral sinus through the teeth of the pectinate ligament stays there in contact with a rich network of vessels, which are part of the anterior ciliary system. These intrascleral vessels (fig. 2 *A*, *In Px*) form a dense plexus, many of the superficial branches of which run at the outer side of the trabecula (*TrV*), their inner wall being in contact with the aqueous through the meshes of the trabecula (trabecular veins). These vessels have been

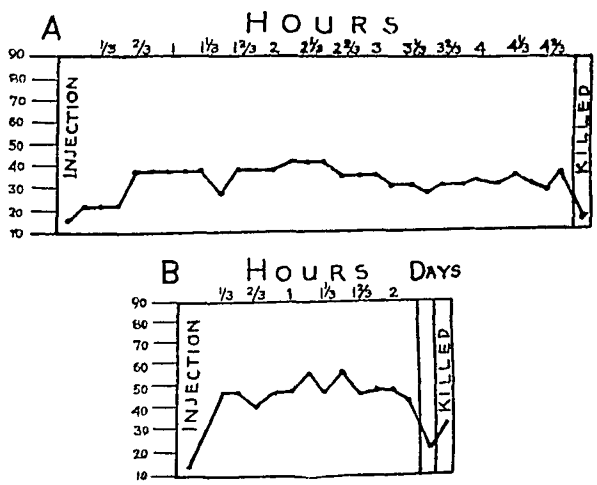

Fig. 3.—Tonometric curves for rabbit 49. *A*, right eye, and *B*, left eye.

compared by former authors to the canal of Schlemm; but, as I have shown elsewhere, there is no canal of Schlemm in lower mammals, and the whole cilioscleral sinus should be considered equivalent from the physiologic standpoint to the canal of Schlemm. At the inner wall of the sinus there are in the ciliary body some vessels, but they do not come superficially in contact with the aqueous. Besides, the hydrostatic pressure of the blood inside them is probably much higher, and they take little part in the outflow of the aqueous.

In monkeys and in man a new organ appears: the canal of Schlemm (fig. 2 *B*), which always occupies the same anatomic place between the

end of Descemet's membrane, high at the upper limit of the trabecula, and the insertion of the ciliary body into the spur. The aqueous is in contact only with the inner wall of the canal of Schlemm, and not with any other vessel of the intrascleral plexus, which runs deep inside the sclera (fig. 2, *In Px*). The canal of Schlemm communicates with the venous plexus only by a few narrow branches, which are called "collectors." The blood does not usually penetrate into the lumen of the canal of Schlemm, as is shown in the normal human eye by gonioscopic inspection.

away, at the inner surface of the cornea, in order to produce a corneal tunnel. This will close the anterior chamber by pressure from within after the injection is made. The aqueous humor is first withdrawn with a sterile syringe; then, with the needle left in place, another syringe is filled with blood and connected with the needle. The injection is made slowly until an amount about the same as that of the aqueous withdrawn is introduced into the chamber. For this maneuver a two way cock attachment is also advantageous. The needle inside the cornea should not be moved in any way, as this widens the puncture and facilitates the leaking of the blood. When the blood flows out from the anterior chamber, incalculable differences may arise in the amount of hypertension.

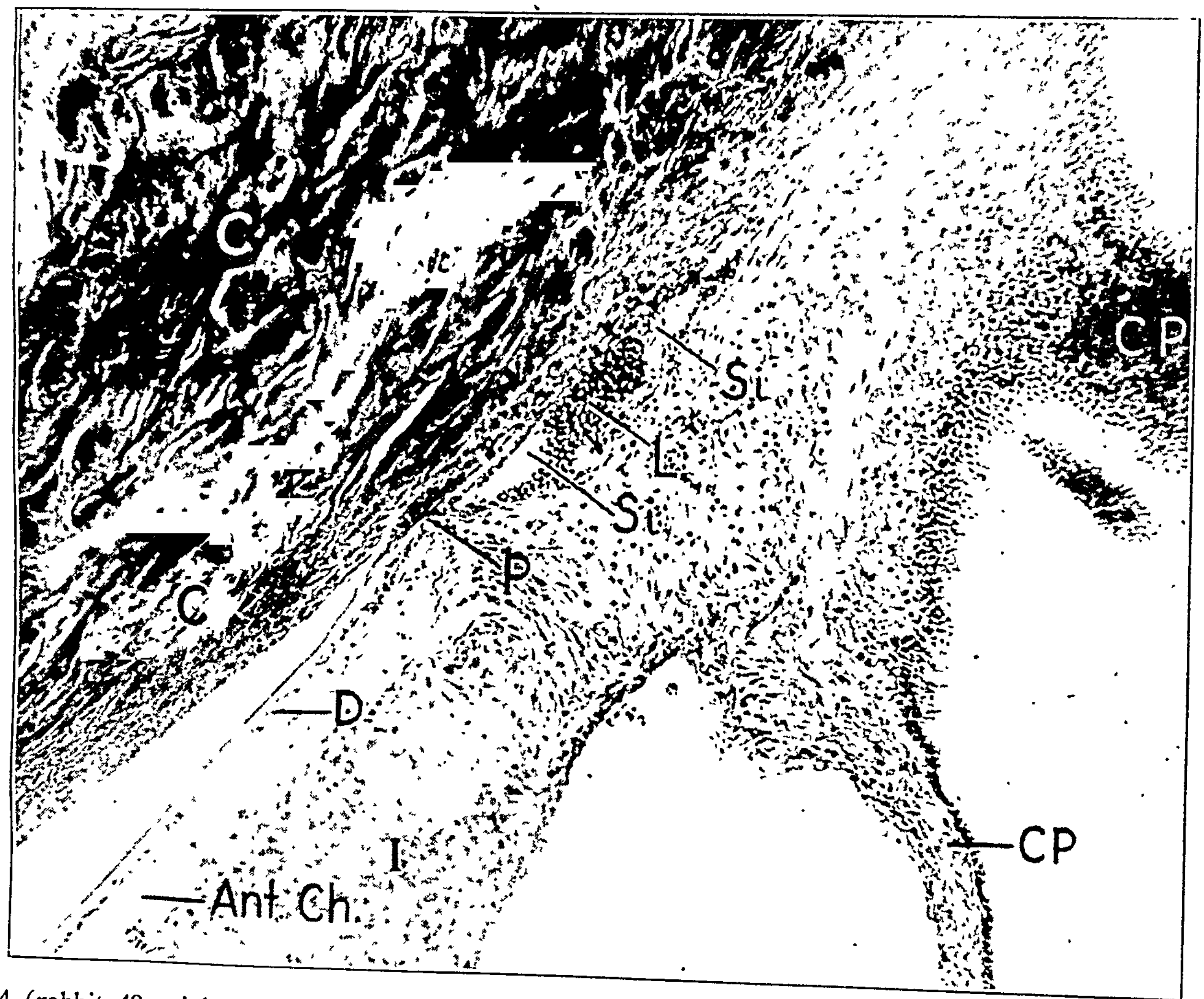

Fig. 4 (rabbit 49; right eye).—Response to the injection of blood serum. *D*, Descemet's membrane, separated from the cornea by an artefact; *Ant Ch*, anterior chamber; *L*, clump of leukocytes inside the sinus, and *CP*, ciliary processes.

TECHNIC OF INJECTION OF SERUM AND BLOOD INTO THE ANTERIOR CHAMBER

The animals were anesthetized either by the method of intraperitoneal injection of pernoston sodium or by ether inhalation. They were also tied securely to special supports for rabbits, dogs or monkeys. In addition, I used a retrobulbar injection of 2 per cent procaine hydrochloride, which is useful in obtaining complete anesthesia of the globe.

To make a perfect injection into the anterior chamber and to avoid the outflow of the injected liquid when the needle is withdrawn, it is necessary to follow a special technic. A needle, 25 gage, is pushed obliquely from the limbus of the cornea into the thickness of the corneal lamella, and a counterpuncture is made far

EXPERIMENTS WITH BLOOD SERUM

Blood taken from the rabbit's heart was centrifuged and the serum, in a sterile condition, injected into the anterior chamber, which had been previously emptied. Two rabbits and 1 dog were employed. Tonometric readings were taken every ten minutes after the injection. Usually the eye became congested, and there was slight chemosis around the limbus. The pupil became smaller. The intraocular tension began to increase about twenty-five minutes after the operation. In rabbit 48 it increased to a considerable height, reaching 65 mm. at the

end of one and three-quarters hours. In rabbit 49, in which operation was performed on both eyes, the tension increased in the right eye to 43 mm. and stayed at about 30 mm. for three and one-half hours after the operation (fig. 3 *A*). In the left eye it reached 55 mm. and next day returned to normal (fig. 3 *B*).

Rabbit 49.—*Pathologic Study*.—Right Eye The eye was enucleated twenty-eight hours after injection (fig 4). The angle was filled with serum. There was some reaction, involving especially lymphocytes, polymorphonuclears and neutrophils. The leukocytes were accumulated in the cilioscleral sinus, *Si* The anterior chamber on the dependent side contained serum, fibrin and scattered leukocytes. The iris, *I*, was somewhat thickened and had a considerable number of dilated vessels. The ciliary processes, *CP*, were normal.

Left Eye: Examination was made two days after injection (fig. 5). The cornea, *C*, was slightly ectatic There was still a layer of serum and fibrin, *Ser*, in the anterior chamber and on the surface of the iris, *I*. The angle of the anterior chamber was normal in the upper part of the eye, but in the dependent part the iris was close to the cornea and was attached to it by a fibrous layer of proliferating endothelium, *P end* (beginning peripheral synechia). The cilioscleral sinus, *Si*, was filled with serum and migrating leukocytes. The iris, *I*, was thicker; its blood vessels were dilated, and it was covered on the anterior surface by a layer of fibrin. The processes, *PC*, were normal.

Dog 1.—Serum was injected into the anterior chamber of both eyes. Microscopic examination revealed changes similar to those in the rabbit.

Pathologic Changes—Left Eye (fig. 6). Blood and serum filled the sinus, *Si*, and the spaces between the fanlike fibers of the pectinate ligament, *P*. The iris, *I*, was thicker than normal. The vessels were dilated, and there was considerable edema in the interstices of the stroma. In some of these interstices there were also blood cells, which were similar to those in the anterior chamber, their presence indicating some absorption of the injected fluid by the iris.

Right Eye: The lesions in the iris were similar to those in the other eye, and the edema of the stroma was considerable. Many pigmented globules were scattered between the fibers of the pectinate ligament. The ciliary processes were normal.

Fig 5 (rabbit 49; left eye).—Response to injection of blood serum. *Ser*, layer of serum and fibrin in the anterior chamber and on the surface of the iris, *I*; *P end*, end of proliferating endothelium, binding the iris to the cornea, and *F*, layer of fibrin.

EXPERIMENTS WITH DEFIBRINATED BLOOD

Blood was taken directly from the heart of the rabbit, defibrinated and immediately injected into the anterior chamber. The aqueous had previously been withdrawn. After the injection the animal was placed with the injected eye uppermost, and tonometric readings were made every ten minutes. Observations were made from time to time to ascertain whether the blood had been already coagulated. Six rabbits and 1 rhesus monkey were used in the experiments. The rabbits were killed one hour, twenty-four hours and two, four, five and sixteen days respectively after the injection.

Rabbit 42.—The animal was killed one hour after the injection. The anterior chamber was well filled with blood. Hypertension reached a high level, 85 mm., as shown in the curve (fig. 7).

Pathologic Changes (fig. 8).—The angle and the cilioscleral sinus, *Si*, were entirely filled with blood, but their normal arrangement was preserved. The sinus was distended on one side. The iris, *I*, was congested. The processes, *CP*, were swollen. The vessels, *V*, were dilated, especially the intrascleral and episcleral veins, *Ev*. However, no reaction or phagocytic migration had yet occurred.

Rabbit 39.—The animal was killed twenty-four hours later. There was chemosis of the limbus, which became severe about one hour after injection. The blood inside the chamber became blacker about one-half hour later, but it was not yet coagulated. An air bubble left inside still moved with the changing of the eye's position. The next day chemosis was still present. The hypertension, which reached 60 mm., fell to 40 mm. in twenty-four hours (fig. 9).

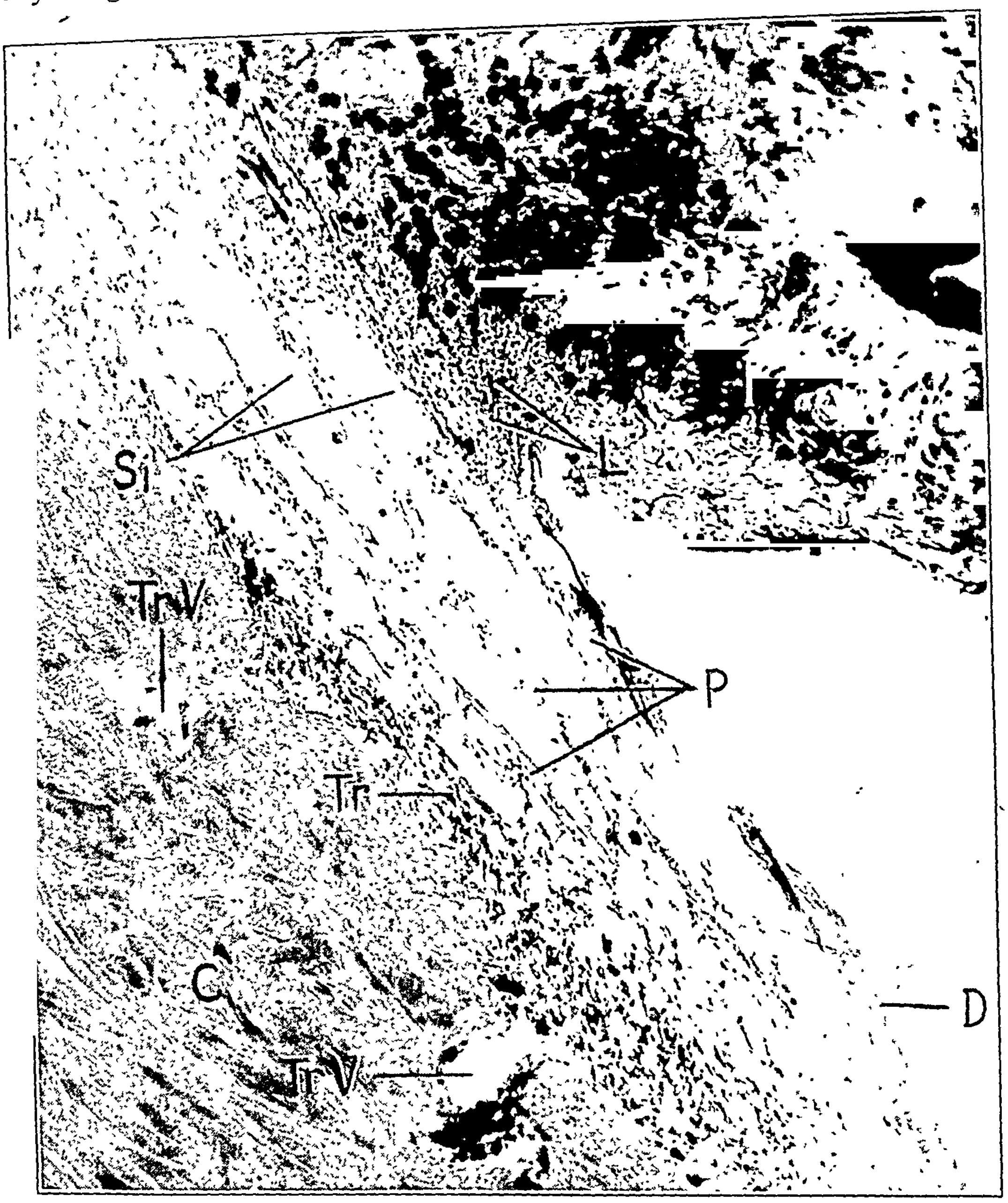

Fig. 6 (dog 1; left eye).—*P*, fanlike fibers of pectinate ligament; *L* clump of leukocytes.

Pathologic Changes (fig. 10).—The central portion of the cornea showed marked necrobiosis, the result of the high tension, which was similar to the condition observed in man. The cilioscleral sinus, *Si*, was occluded on both sides of the section by apposition of the base of the ciliary body, *BC*, and the root of the iris, *I*, against the sclera, *S*. This condition may be aptly designated as sinus synechia. The iris was greatly thickened, and its vessels were much dilated. Serum was present in the interstices of the stroma of the iris. The processes, *CP*, were greatly swollen. On the dependent side, blood had infiltrated between the sclera and the ciliary body. There was early prolifera- tion of the endothelium, more pronounced in the cornea than in the iris, but little phagocytic migration. The

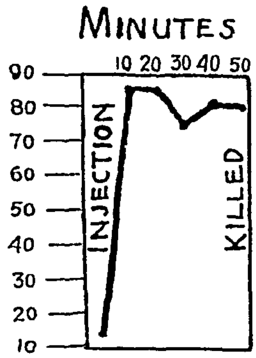

Fig. 7.—Tonometric curve for rabbit 42.

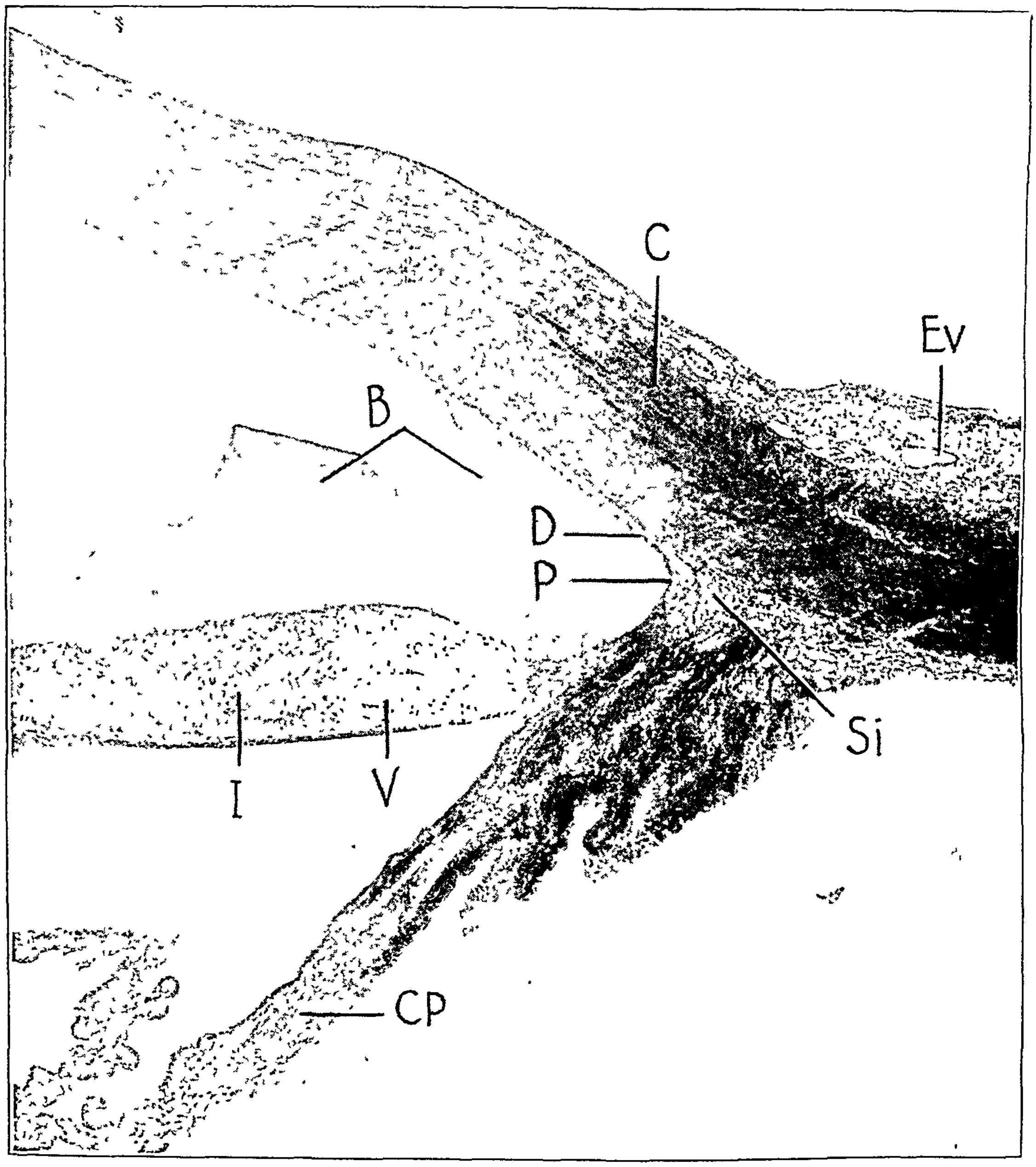

Fig. 8 (rabbit 42).—Response of injection of defibrinated blood into the anterior chamber. *B* indicates blood in the anterior chamber, which also fills the cilioscleral sinus; *D*, end of Descemet's membrane; *CP* ciliary processes, and *EV*, episcleral vessels.

corneal membrane had begun to dilate. The conjunctival and intrascleral vessels, *Ev,* were greatly dilated.

RABBIT 44.—The animal was killed two days after injection. The eye became congested and chemotic fell the next day to 45 mm. and was 35 mm. when the animal was killed (fig. 11).

Pathologic Changes (fig. 12).—The cornea, *C,* was much dilated at the limbus, and there was slight necrobi-

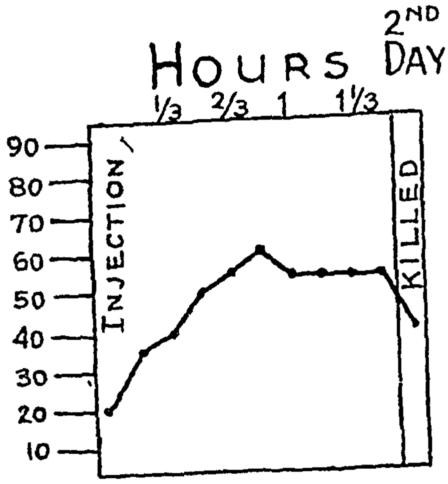

Fig. 9.—Tonometric curve for rabbit 39.

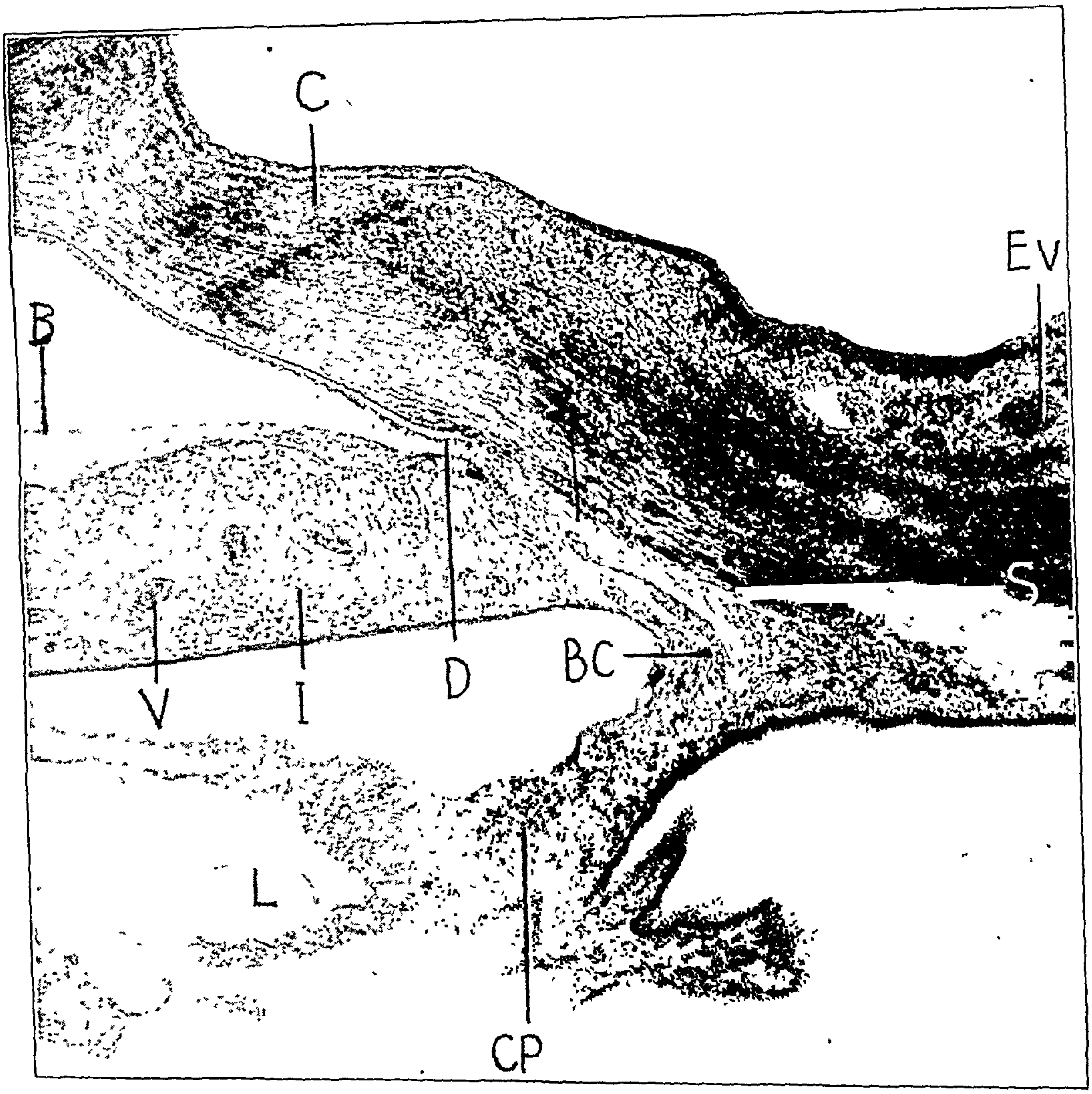

Fig. 10 (rabbit 39).—*B,* blood in the anterior chamber and on the surface of the iris; *I; Bc,* base of ciliary body; *CP,* ciliary processes; *L,* Graefe's blebs and *EV,* episcleral vessel.

soon after the injection. The cornea began to dilate forty-eight hours later. A red and white clot was still present in the anterior chamber when the animal was killed. The tension reached the high level of 85 mm. but

osis, in the posterior lamella only. Blood, *Bl,* had infiltrated into the limbus. The sinus, *Si,* was partially infiltrated with blood and was occluded. On the dependent side the root of the iris, *Ir,* was thickened and

obstructed the sinus, which was partly filled with blood. The processes, *CP*, were greatly swollen, so that they pushed the root of the iris against the cornea and gave rise to a true anterior peripheral synechia. There was an enormous increase in the number of vessels in the iris, *V*, which were filled with leukocytes. Also present needle, and there was leaking of the blood when the needle was withdrawn. The eye, however, became congested and chemotic. The cornea was ectatic on the second day. Tension rose to 85 mm. and fell to 28 mm., continuing at the same level until the animal was killed (fig. 13).

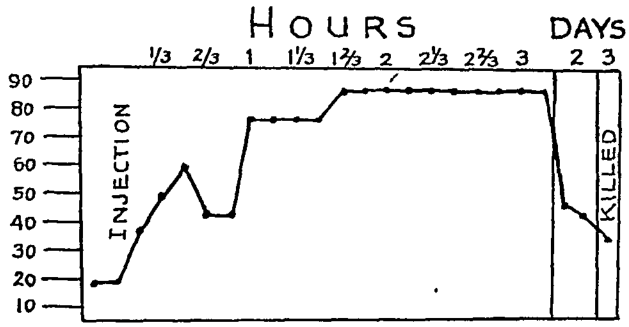

Fig. 11.—Tonometric curve for rabbit 44.

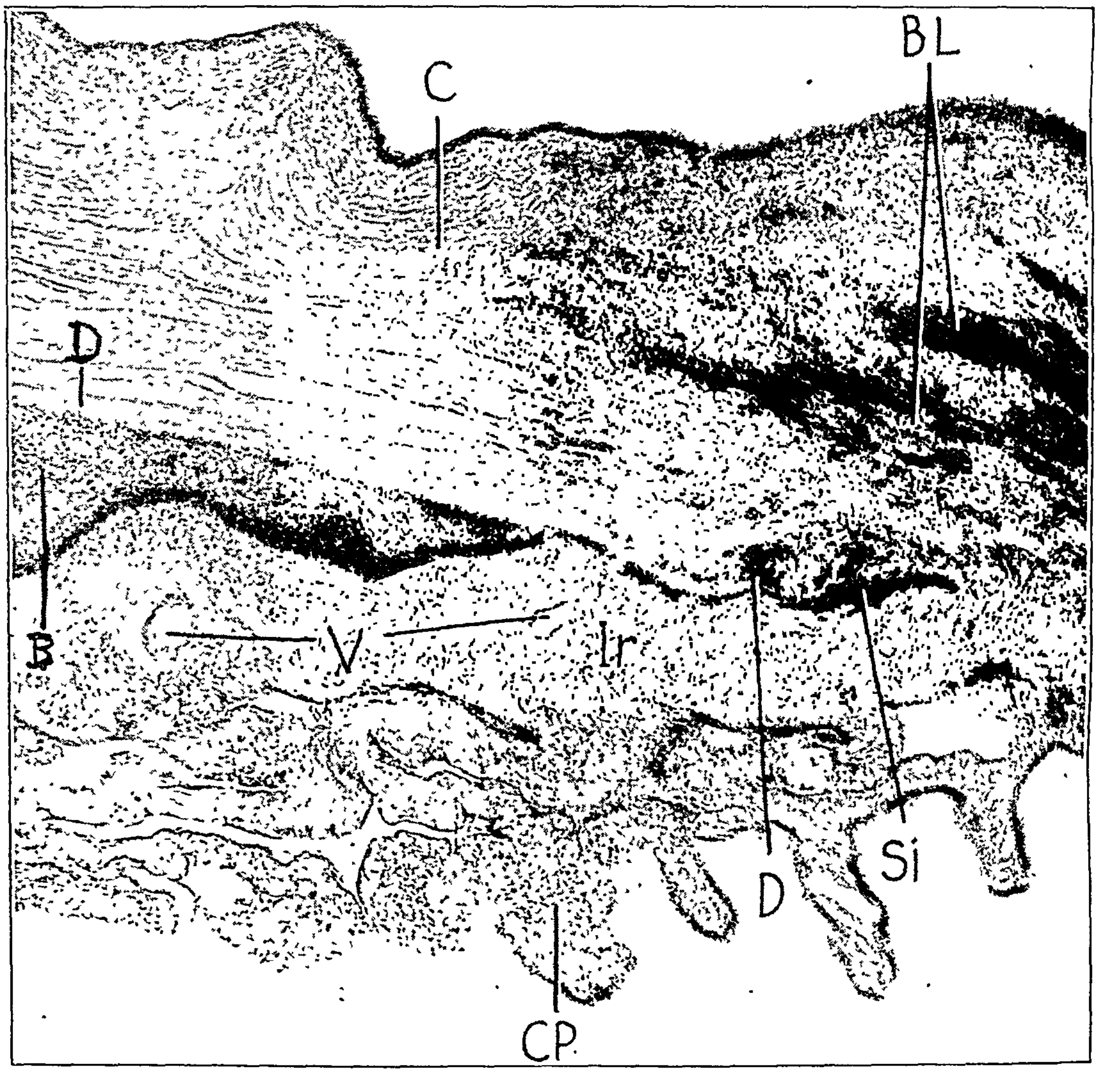

Fig. 12 (rabbit 44).—*BL,* blood infiltrating the limbus; *Si,* cilioscleral sinus, filled with blood; *Ir,* root of the iris, pushed forward by swollen ciliary processes, *CP,* forming an anterior peripheral synechia; *V,* vessels of the iris, and *B,* blood in the anterior chamber.

was notable proliferation of the corneal endothelium at the angle, due to irritation, and the leukocytic reaction was more prominent than in rabbit 39. There was a large amount of fluid outside the vessels.

Rabbit 45.—The animal was killed four days after the injection. Movements of the animal displaced the

Pathologic Changes (fig. 14).—The cornea, *C,* was considerably thicker in the center, due to edema. It was also ectatic. Four new blood vessels appeared, filled with granules of hemosiderin—some phagocytosed and some free—at the limbus and in the central portion of the cornea. The sinus, *Si,* was free on both sides. The

swollen root of the iris, *Ir,* was attached to the cornea at the end of Descemet's membrane, *D,* free communication with the anterior chamber being thus prevented. Blood was still present in the chamber. The iris, *I,* in the cornea. The processes, *CP,* were congested and in contact with the anterior surface of the lens. They seemed to be pushing the root of the iris outward. The choroid was not congested.

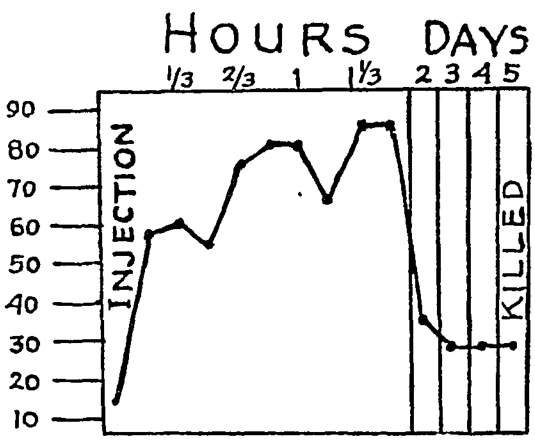

Fig. 13.—Tonometric curve for rabbit 45.

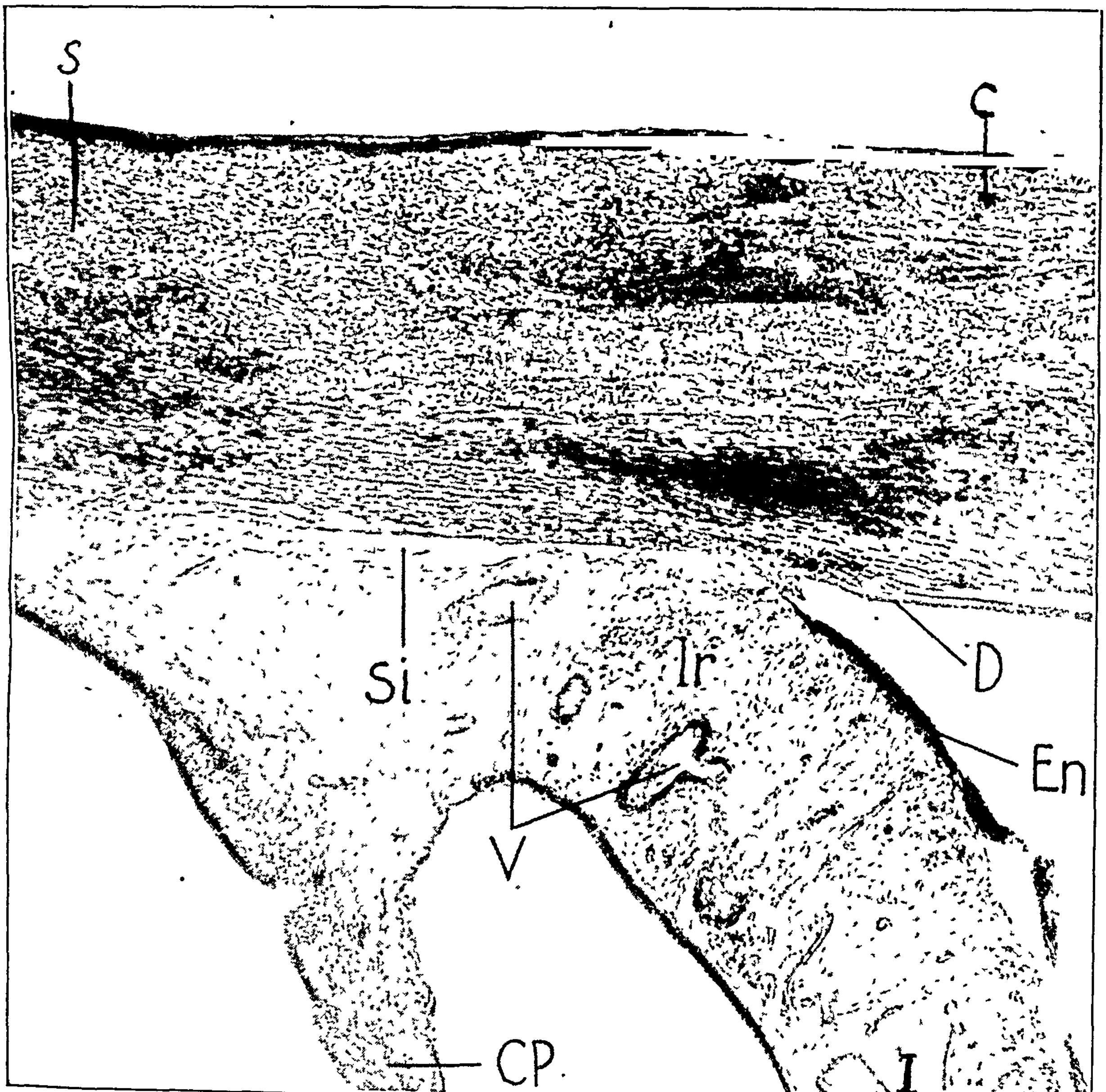

Fig. 14 (rabbit 45).—The abbreviations have the same meaning as in figure 12. *En* indicates endothelial proliferation over the surface of the iris.

was greatly thickened. There was still great vascularity, but the vessels, *V,* did not contain leukocytes, as in rabbit 44. Few leukocytes were present in the stroma of the iris. There was an increase in endothelial proliferation, *En,* and fibrous tissue in the iris, with less

Rabbit 36.—The animal was killed five days after injection. Two hours after the injection the eye was red and chemotic. The next day the cornea was clear, and the blood was absorbed over the iris but still remained over the pupil. A white clot or exudate lay

below and outside the pupil, reaching the angle. Tension attained a level of 85 mm. and lasted until the fifth day, when it was 30 mm. (fig. 15).

Pathologic Changes (fig. 16).—The eyeball was dilated as a whole, but the cornea was wrinkled. No necrobiosis of the cornea was present. A hemorrhage occurred near the limbus in the upper part. The sinus, *Si*, was filled up with fibrous tissue, *F*, which extended along the posterior surface of the cornea, between it and the iris, outside the peripheral synechia, *Psy*, and beyond it, as a result of organization of exudate. The iris, *Ir*, was less swollen. The vessels, *V*, were dilated, containing more blood. On the dependent side the same condition was present, but the iris had retracted and, detaching itself from Descemet's membrane, formed a pathologic angle. Endothelial proliferation occurred chiefly in the cornea, and to a less extent in the iris. The choroid was greatly congested.

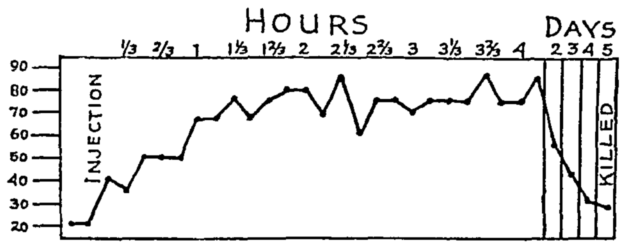

Fig. 15.—Tonometric curve for rabbit 36.

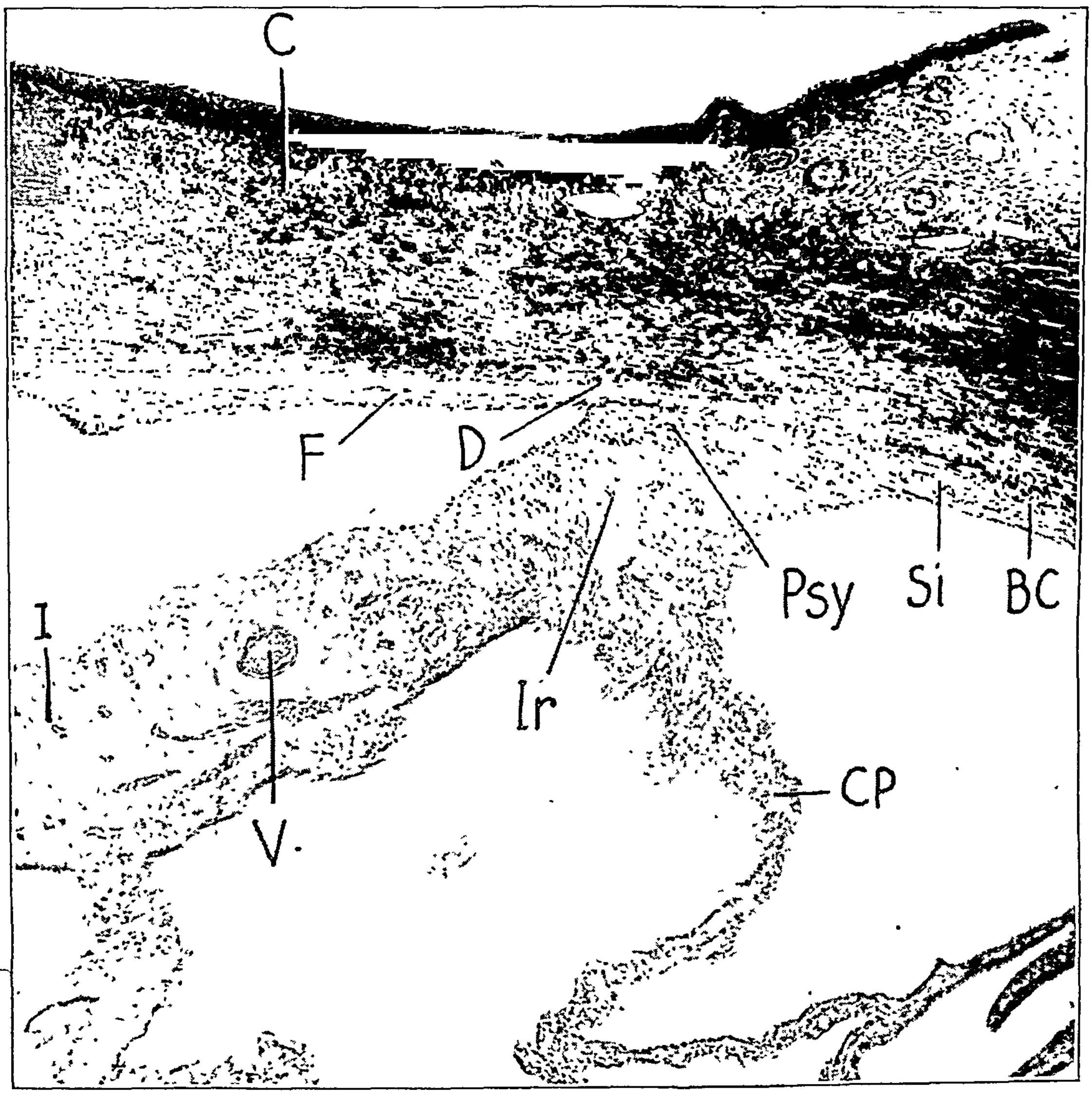

Fig. 16 (rabbit 36).—*BC* indicates base of ciliary body; *Ir*, root of iris, pushed forward; *Psy*, anterior peripheral synechia; *F*, fibrous tissue, forming a wedge between Descemet's membrane and the synechia; *I*, iris, with its vessels, *V*, greatly congested, and CP, ciliary processes.

Rabbit 37.—The animal was killed sixteen days after the injection. Chemosis was present at the end of the first hour. The next day the blood still covered the iris. The pupil, however, was visible. The cornea was slightly opaque and injected. Five days later the blood had become almost entirely absorbed in the anterior

chamber and over the iris. The pupil was dilated, non-active and irregular. New vessels were present on the surface of the iris. On the sixteenth day, when the animal was killed, the anterior chamber became shallow. Tension, which reached 85 mm. after injection, fell to 30 mm. the next day and remained so for the entire period of the experiment (fig. 17).

Pathologic Changes (fig. 18).—The cornea, *C*, showed newly formed vessels, containing leukocytes. No trace of blood was present in the anterior chamber. The sinus, *Si*, was closed by the root of the iris but still showed a few open spaces. The root of the iris, *Ir*, was retracted from the end of Descemet's membrane, *D*, by fibrous tissue. The iris, *I*, was still thicker near the pupil but was thinner and more atrophic at its base. The whole base of the ciliary body, *BC* was atrophic, although some processes, *CP*, were still swollen. Numerous dilated vessels showed sclerosis of their

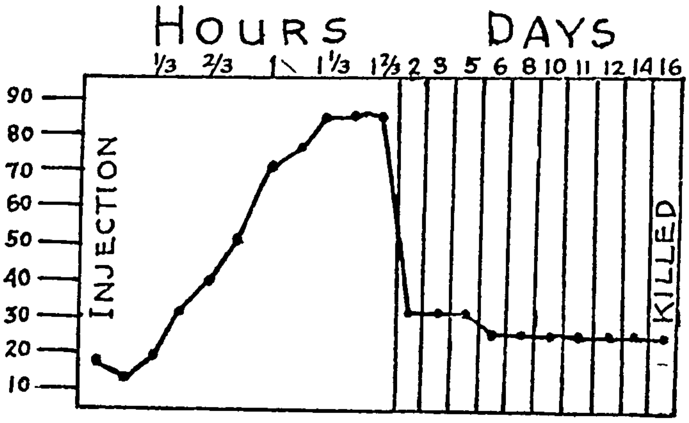

Fig. 17.—Tonometric curve for rabbit 37.

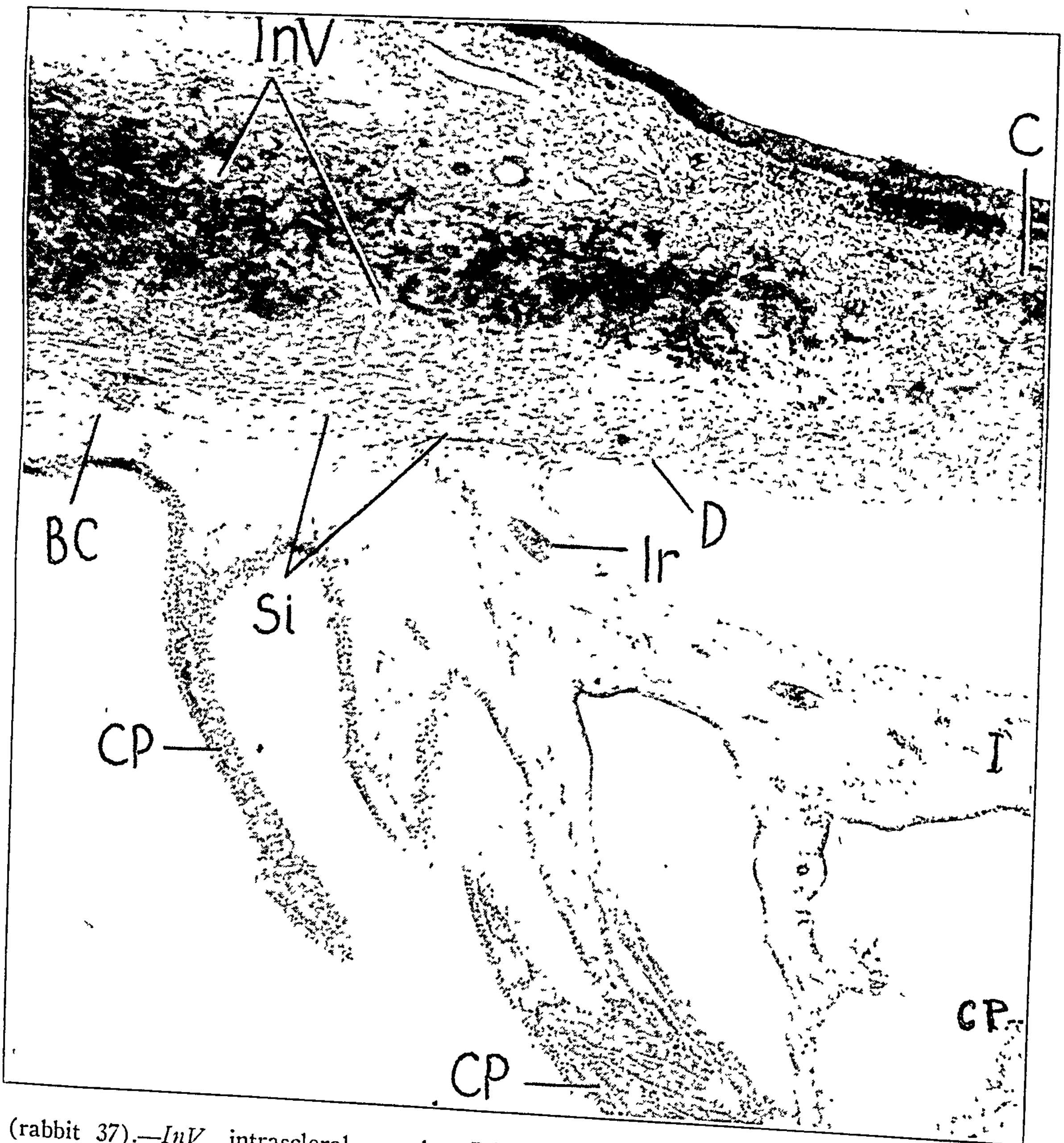

Fig. 18 (rabbit 37).—*InV*, intrascleral vessels; *BC*, base of ciliary body; *Ir*, root of the iris; *D*, end of Descemet's membrane, and *CP*, ciliary processes.

walls. The choroid was enormously congested. The intrascleral veins, *In V,* were also greatly congested.

Rhesus Monkey 1.—The right eye of this animal was given an injection first and the left eye twenty-four hours later. The animal was killed five and a half hours after the injection into the left eye.

Left Eye.—Chemosis started in the left eye a half-hour after the injection. Four hours later the iris became visible, the blood being rapidly absorbed from the angle to the center. After five and a half hours there was still blood in the chamber. Tension reached 67 mm. and fell to 58 mm. when the animal was killed (fig. 19).

Pathologic Changes (fig. 20).—The animal was killed five and a half hours after the injection. The left eyeball was greatly dilated; it was triangular, with the cornea at the apex. The anterior chamber was deep. There was blood in the angle, filling the trabecula, *Tr,* which with the canal of Schlemm, *Sch,* had preserved its normal aspect. The iris was edematous; the vessels were dilated, and the choroid was ectatic. No reaction had yet occurred.

Right Eye.—In the right eye, immediately after injection, the blood filled the anterior chamber, and there was slight chemosis. Two hours later the pupil became visible. One day later the chemosis was greatly increased. The blood in the anterior chamber was absorbed at that time. Tension rose to 80 mm., with oscillations, and the next day fell below normal (fig. 21).

Pathologic Changes: The changes were similar to those observed in the left eye. The cornea was normal. The eye was dilated, with scleral, followed by choroidal, ectasia. Hemorrhage was present inside the limbus. In the angle, the trabecula was somewhat distorted, containing blood and partially narrowing the lumen of the canal of Schlemm on one side. The trabecula contained blood but no leukocytes. The iris was thickened and edematous. The vessels were congested and dilated, and the processes were normal. The tolerance of this eye is remarkable as compared with the eye of the rabbit.

Résumé of Pathologic Observations.—During the first hour after the injection of defibrinated blood in the anterior chamber, the fluid entirely filled the cilioscleral sinus on both sides and produced a great neurovascular response, but with no phagocytic reaction as yet. Ten minutes after the injection extreme hypertension appeared (measuring 85 mm.), which was due to the mechanical filling of the sinuses with blood. At this time there was no peripheral synechia (fig. 8).

At the end of twenty-four hours (fig. 10) the blood had beeen absorbed inside the sinus, but the enormous thickening of the root of the iris and the base of the ciliary body had produced mechanical closure of the sinuses. The angle of the chamber between the iris and the end of Descemet's membrane was open. As the intrascleral vessels, which normally absorb the greater part of the aqueous humor, were covered by the root of the iris and the base of the ciliary body, no absorption of fluid could be produced This adhesion is a new form of peripheral synechia, which may be called sinus synechia. At this time the leukocytic reaction was considerable, and there was also early proliferation of the endothelium, both of the cornea and of the iris.

Forty-eight hours later (fig. 12), in addition to obliteration of the sinus, the root of the iris had encroached on the anterior chamber, covering the end of Descemet's membrane, which in the normal rabbit eye marks the limit of the chamber. A true anterior peripheral synechia was thus produced, undoubtedly due in great part to the swelling and thickening of the processes, which pushed the root of the iris, and even part of its surface, against the cornea. The anterior chamber became shallow as a result of this pressure. The two reactions, leukocytic and endothelial, were pronounced. There was also a large amount of fluid outside the vessels.

Four days later (fig. 14) the small amount of blood injected had been absorbed on the sinus, which could be seen to have partly reopened. However, hypertension was still present, as a result of the adhesion of the root of the iris to the sclera, which cut off the communications between the anterior chamber and the sinus. The iris and processes were greatly swollen and the vessels in the iris much dilated, but they did not contain as many leukocytes as at the end of twenty-four hours. On the other hand, the endothelial reaction had increased. There were endothelial proliferation and formation of fibrous tissue in the iris.

Five days later (fig. 15) the most striking symptom was the great dilatation of the whole eyeball. The sinuses were entirely filled with fibrous tissue, the result of organization of exudates. A true peripheral synechia was also present, the root of the iris covering a great extent of Descemet's membrane. The iridic membrane was less swollen. Endothelial proliferation continued chiefly in the cornea and to a less extent in the iris.

Sixteen days later (fig. 18) no trace of blood was observed in the anterior chamber. There was a sinus synechia but no peripheral synechia, the iris being retracted from the end of Descemet's membrane by the formation of fibrous tissue. The root of the iris and the base of the ciliary body were atrophic—a retrograde process similar to the condition seen in the human eye with long-standing glaucoma. However, at the end of two weeks there was still congestion of the eye.

The eye of the rhesus monkey (fig. 20) presented a different reaction to the injection of blood than did the rabbit eye. The absorption was so rapid that at the end of five and a quarter hours little blood was left in the chamber. Some

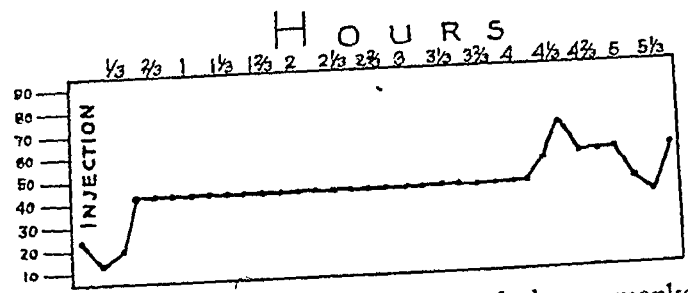

Fig. 19.—Tonometric curve for left eye of rhesus monkey 1.

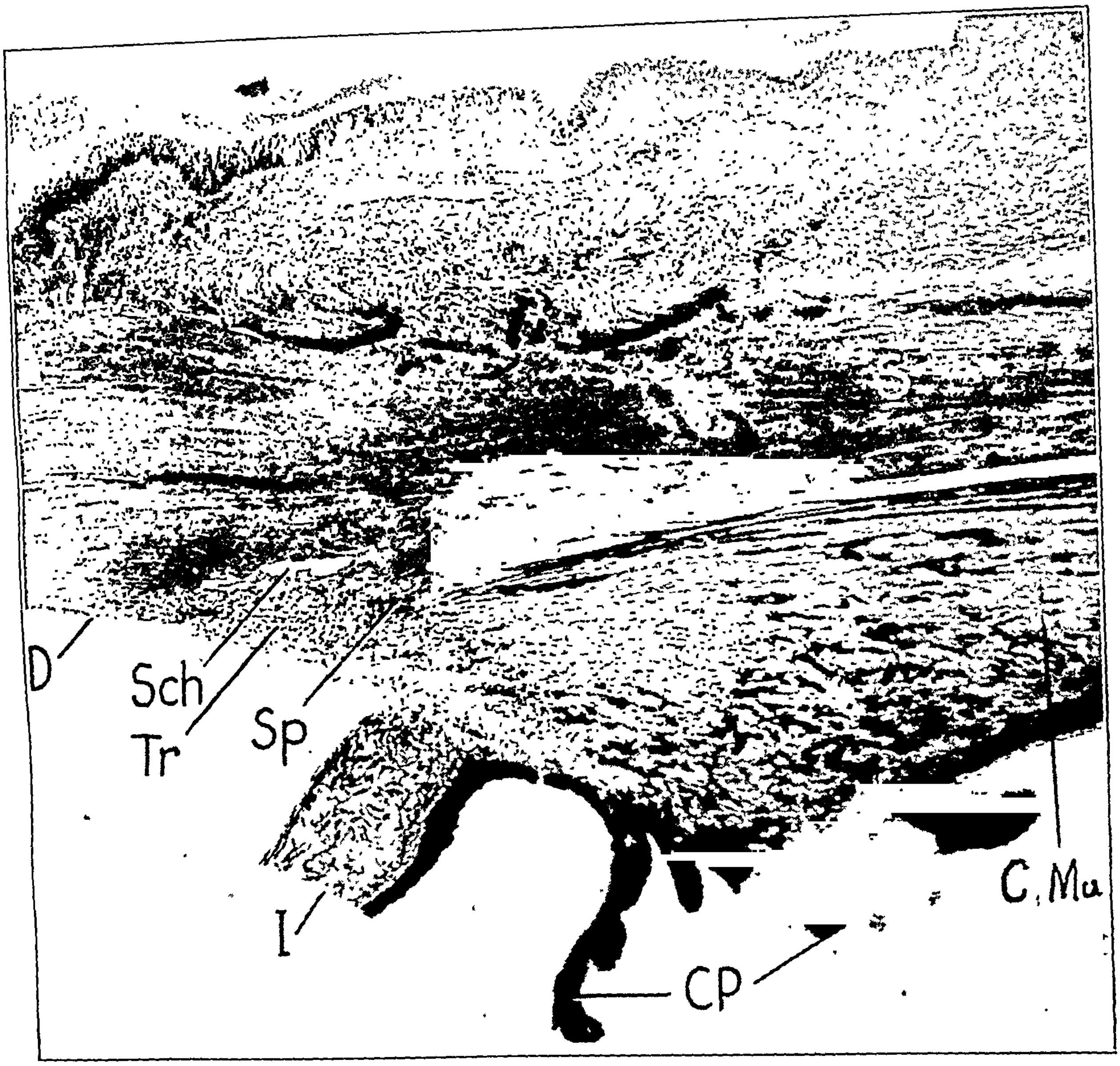

Fig. 20 (rhesus monkey 1; left eye).—*Sch.* canal of Schlemm; *C Mu,* ciliary muscle; *CP,* ciliary processes, *Sp,* scleral spur.

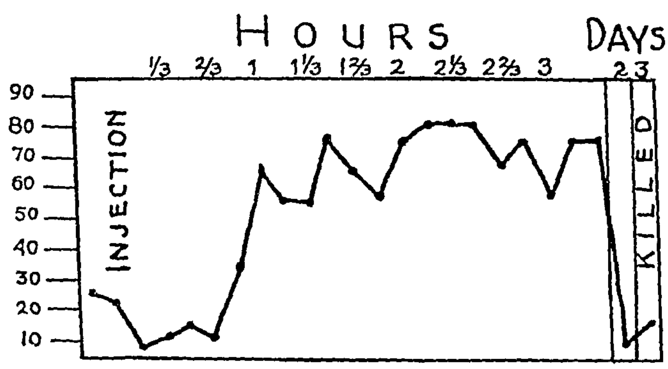

Fig. 21.—Tonometric curve for the right eye of rhesus monkey 1.

corpuscles filled the trabecula, which, with the canal of Schlemm, had a normal structure. Still, tension reached nearly 70 mm. The iris was edematous, with a great number of dilated vessels, but there was no leukocytic reaction. In of Schlemm narrowed. The leukocytic reaction was slight. The iris was thickened and edematous, with congested vessels. The tolerance of this monkey's eye to the injection of blood was remarkable.

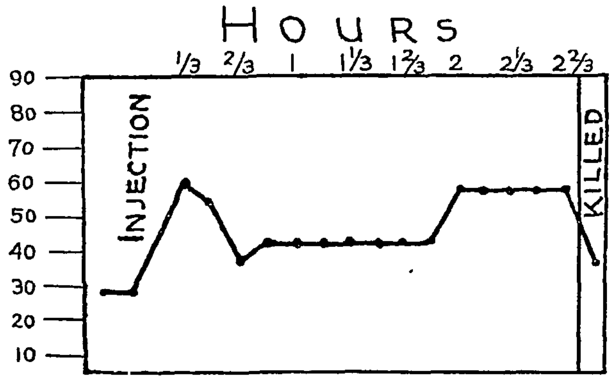

Fig. 22.—Tonometric curve for rabbit 30.

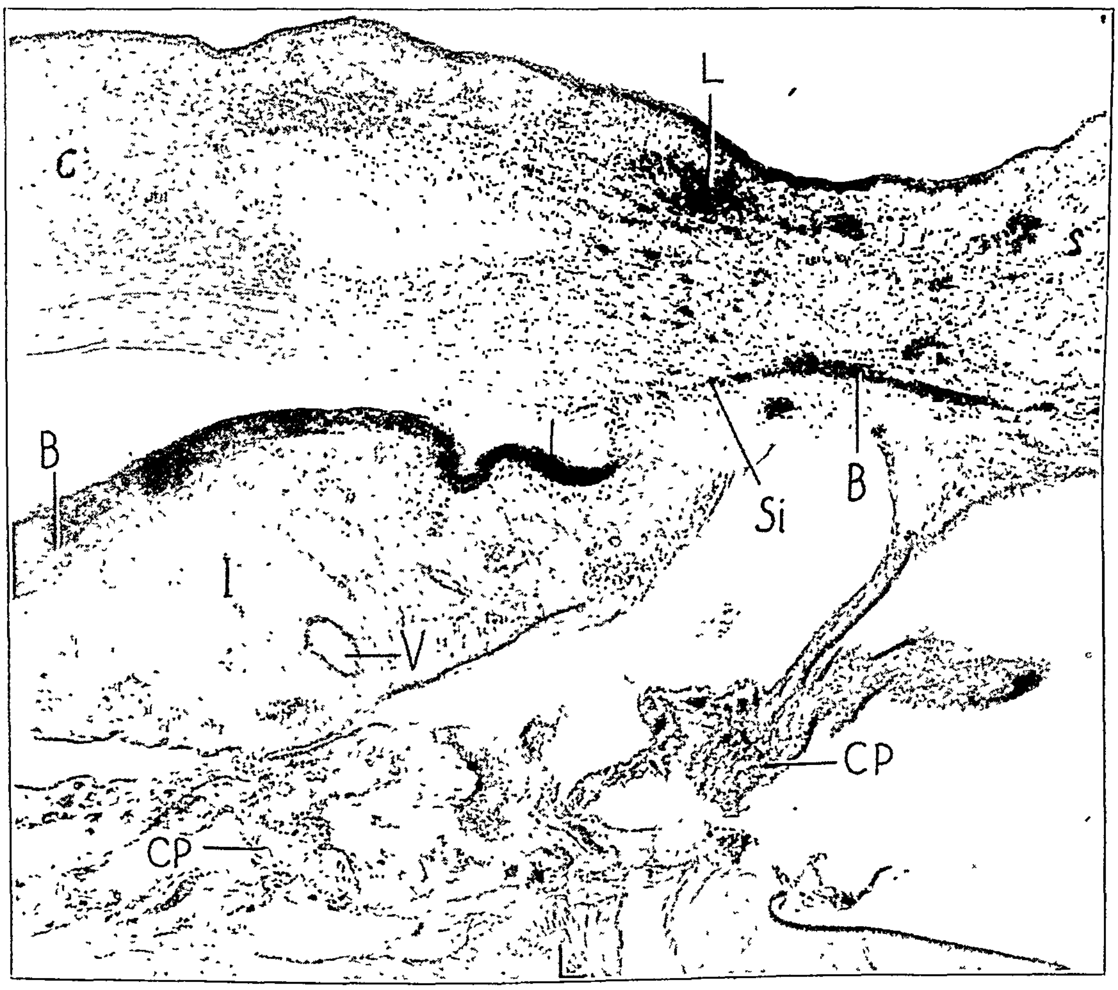

Fig. 23.—*L,* clump of leukocytes; *B,* blood filling the sinus and infiltrating the sclera and subchoroidal space; *I,* iris, covered with blood, *B;* *V,* dilated vessel in the iris; *CP,* ciliary processes, and *L,* lens.

the other eye, after forty-eight hours the dilatation of the whole eyeball was extreme. The tension increased more rapidly than in the rabbit. Tension had fallen to normal, although the trabecula was somewhat disturbed and the canal

The dilatation of the cornea and of the whole eyeball in animals usually produces a rapid descent in intraocular pressure on the second or the third day. It is probable that if the sclera were as resistant as it is in man, a condition

which clinically and pathologically resembled glaucoma in man would be produced.

EXPERIMENTS WITH PURE BLOOD

The anterior chamber was emptied by the withdrawal of the aqueous with a fine needle and the chamber. After the injection the animal was placed at rest on the side opposite that of the eye operated on. Reaction did not usually appear until fifteen or twenty minutes had elapsed. When the injected blood filled the anterior chamber under pressure, the cornea became

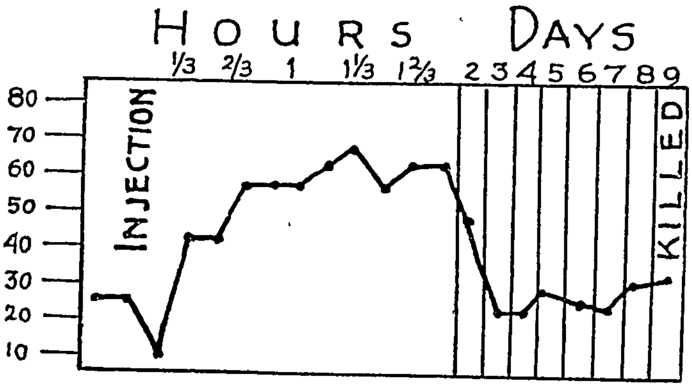

Fig. 24.—Tonometric curve for rabbit 29.

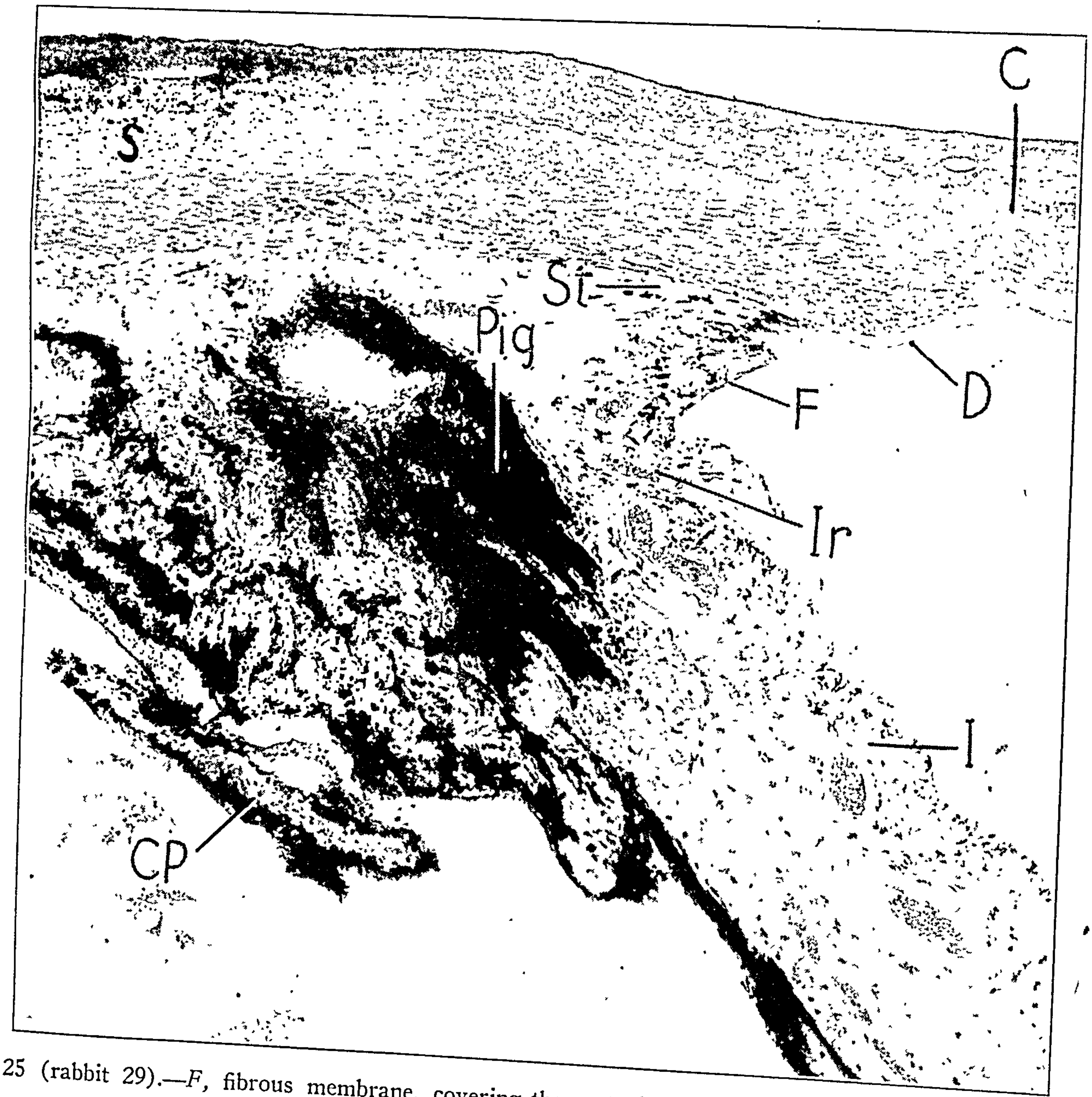

Fig. 25 (rabbit 29).—*F*, fibrous membrane, covering the root of the iris, *Ir*, and *Pig*, collection of pigment.

syringe. The syringe was then removed and the needle kept firmly in place. Another syringe, filled with blood taken directly from the heart of the rabbit, was connected with the needle in opaque and the eye red and chemotic. In 1 rabbit the eyeball burst at the end of ten days, after a large scleral staphyloma had developed. Microscopic section showed a large hemorrhage

in the vitreous and under the choroid. When the injection was made slowly and the pressure was gradually increased, the cornea kept its transparency. The blood apparently clotted in the anterior chamber about half an hour after injection. The tension started to rise ten minutes later, usually reaching a height of 65 to 80 mm. Hypertension lasted for two and a half hours or more, but the next day the tension was much lower and returned to normal, or even below normal. After twenty-four hours the dilation of the cornea and the anterior portion of the eye began. In one week the eye became quiet and redness disappeared, but the anterior segment remained permanently ectatic. Injections were made in 4 rabbits, and the animals were killed twenty-four hours and nine, ten and twenty-three days later.

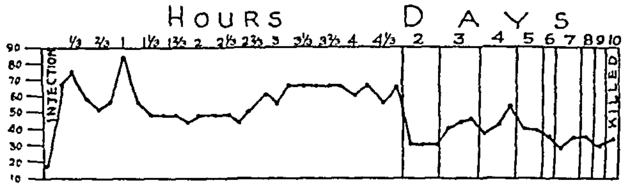

Fig. 26.—Tonometric curve for rabbit 28.

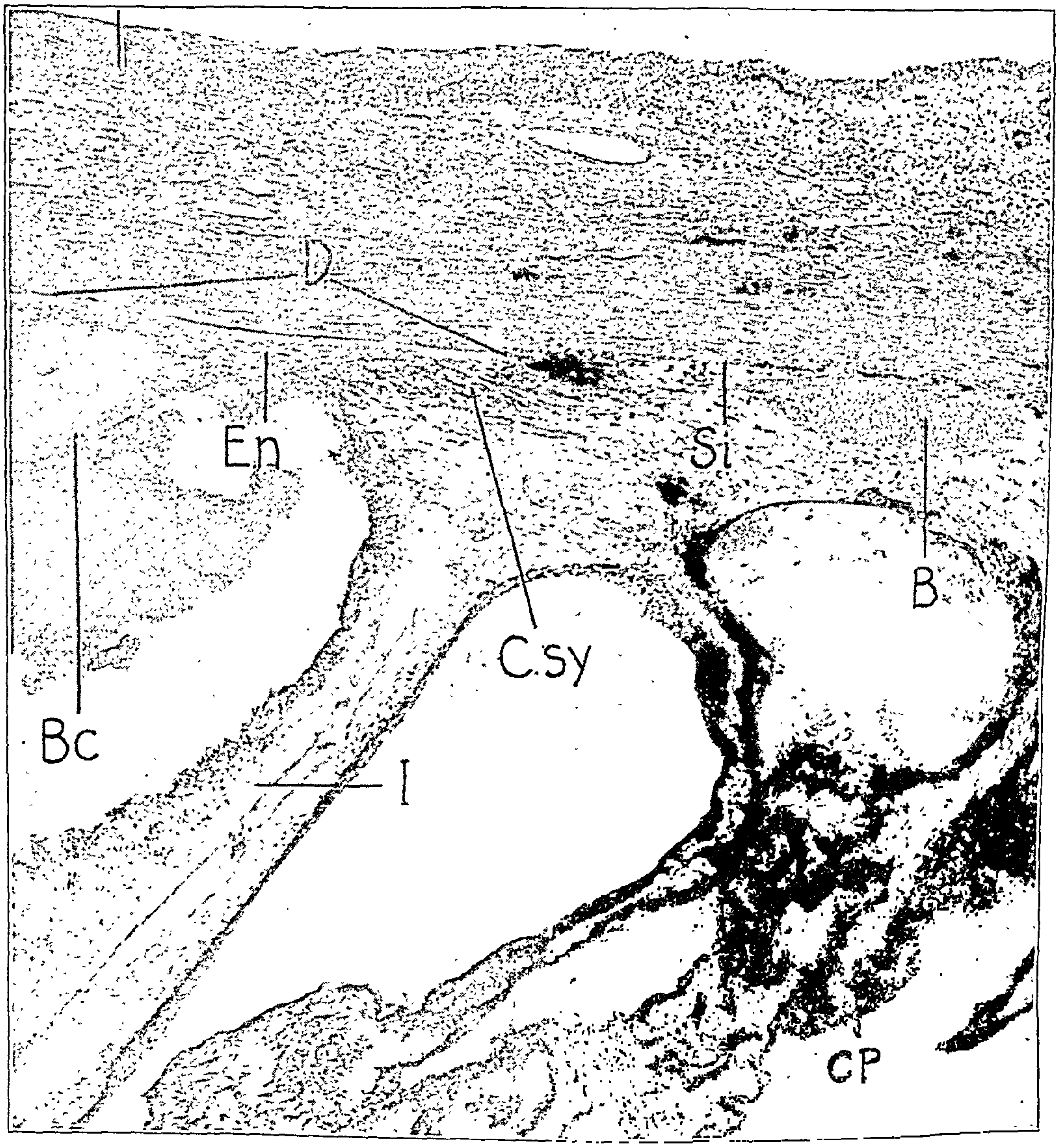

Fig. 27 (rabbit 28).—*Csy*, iridocorneal synechia; *En*, endothelial proliferation, forming a mass between the cornea and the iris and extending in strands around the clot, *BC*.

Rabbit 30.—The animal was killed twenty-four hours after injection. The eye became red and chemotic.

Tension, as shown by the curve (fig. 22), reached a height of 55 mm. and had fallen to 40 mm. two hours later. The next day the eye was congested and the cornea dilated and hazy. The anterior chamber was filled with blood.

Pathologic Changes.—The cornea was edematous. Leukocytes were noted superficially at the limbus. New blood vessels had formed inside the cornea. The anterior chamber showed a thick layer of blood filling the sinus on the dependent side. Blood also infiltrated the ciliary body, reaching the ora serrata. On the other side of the angle (fig. 23), the sinus, *Si,* was filled with blood, *B,* and was occluded by the root of the iris. Beyond, there was a slight infiltration of blood into the ciliary body. The iris, *I,* and processes, *CP,* were greatly congested, and the blood vessels, *V,* were dilated. There was blood over the surface of the iris, *B,* and in the posterior chamber. The lens, *L,* was injured. There was a slight subchoroid hemorrhage. In the iris dispersion of pigment was apparent.

Rabbit 29.—The animal was killed nine days after injection. Chemosis started in the conjunctiva fifteen minutes after the injection and became severe one and a half hours later. Tension reached 65 mm. and fell the next day, but remained higher than normal (fig. 24). Twenty-four hours later chemosis was still present. The blood in the chamber was reduced to hyphemia, with downward extension. Red coloration of the iris was apparent for four or five days. At that time the cornea appeared dilated, ectatic and hazy, and there was a white exudate in the angle. Seven days later the cornea had regained its transparency; but there was still blood in the anterior chamber, and the anterior staphyloma had increased. The animal was then killed.

Pathologic Changes (fig. 25).—The cornea was edematous and thickened. The anterior chamber was deep and contained sparse, individually distributed blood cells. A fibrous membrane, *F,* covered the iris near the angle. The sinus, *Si,* was occluded in front by a sinus synechia up to the end of Descemet's membrane, *D,* but opened backward on each side. There was no peripheral synechia. The iris, *I,* was thick, with dilated blood vessels. The processes, *CP,* were thickened and were adherent to each other. The pigment epithelium, *Pig,* showed great disturbances, with enormous collections in the ciliary body. There were subchoroid hemorrhage and detachment of the choroid.

Rabbit 28.—The animal was killed ten days after injection. Fifteen minutes after the injection chemosis appeared around the limbus; one-half hour later the blood was seen clotting in the anterior chamber, and the clot began to retract. Two hours later chemosis was pronounced. The lids were slightly swollen, and there was a watery discharge from the eye. Tension, which had reached a high level (90 mm.), fell the following day to 35 mm. (fig. 26). At that time chemosis was still present, the cornea being hazy and insensitive. In the anterior chamber the clot had retracted to a brown mass. Seven days after the injection the eyeball was dilated, and an anterior staphyloma of the limbus extended inward and downward. Blood clots were still visible in the anterior chamber over the iris and in the angle. The animal was killed, with the tension still high (35 mm.).

Pathologic Changes (fig. 27).—No necrobiosis of the cornea was evident. There were a sinus *synechia, Si,* with the spaces back of it filled with blood, *B,* and iridocorneal synechiae, *Csy.* These extended beyond the end of Descemet's membrane, *D,* and were broad and permanent. Adjacent to them proliferation of corneal endothelium, *En,* formed a mass over the blood clot, *BC.* In the anterior chamber the endothelium was transformed into strands around the clot. The iris, *I,* was thickened as a result of increase in and dilation of the vessels. Greefe blebs were visible in the process, such as are produced in man by hypotension. The pigment epithelium was disturbed and collected in masses in the processes.

Rabbit 1.—The animal was killed twenty-three days after injection. This animal received two injections of blood. The first one was not successful, as blood came out through the corneal puncture. However, the tension rose to 60 mm. and returned to normal on the next day. The second injection was made six days after the first, and the tension rose to 40 and 50 mm. (fig. 28). The eye remained red, and there was some edema of the lids. The cornea appeared hazy and chemotic. At the end of three days the eyeball became dilated, so that the anterior chamber was deep. Blood remained in the anterior chamber for eighteen days, but was already absorbed on the twenty-third day, when the eye was removed.

Pathologic Changes (fig. 29).—The cornea, *C,* was greatly dilated, and the posterior corneal lamellas were necrobiotic. The sinus was entirely occluded on both sides. The iris, *I,* was atrophic and had receded backward from the end of Descemet's membrane. The processes, *CP,* were also shrunken. Blood, *B,* and hematogenous pigment were present within the synechia, which was fibrous and permanent. The cornea was greatly dilated, and the anterior chamber was deep.

Résumé of Pathologic Changes.—The reaction of the eye with pure blood was somewhat different than with defibrinated blood. The blood apparently clotted in the anterior chamber about one-half hour after the injection and spread over the surface of the iris. It was not possible to study, as with defibrinated blood, the early cause of hypertension, since the first rabbit was killed twenty-four hours after injection. In this animal (fig. 23) the cilioscleral sinuses were filled with coagulated blood, which on one side reached the ora serrata and on the other trickled into the posterior chamber. The edema of the iris was enormous, probably more than with defibrinated blood; the ciliary body itself was swollen, and a sinus synechia had already developed through complete obliteration of the sinus cavity. The great increase of tension in this eye was essentially due to this mechanical occlusion of the sinus by the blood and by the edema of the base of the ciliary body.

In rabbit 29, after nine days (fig. 25) the cornea was greatly dilated, edematous and thickened. Sinus synechiae, but no peripheral synechiae, existed. The anterior chamber became deeper, an alteration which prevented the processes from pushing the root of the iris against the cornea and accounted for the small peripheral synechiae in rabbit 28 (fig. 27). In this animal the proliferation of the corneal endothelium was extreme, not only at the angle but in strands around the clot remaining in the anterior chamber.

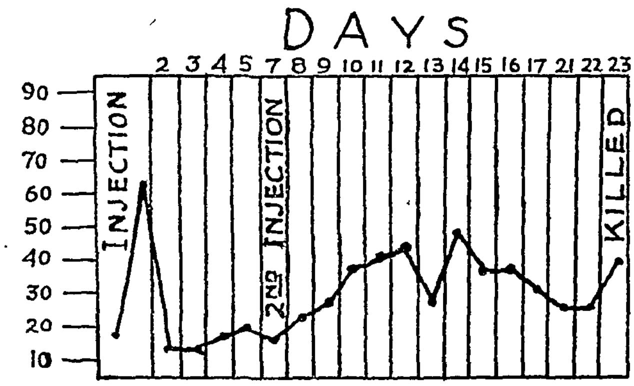

Fig. 28.—Tonometric curve for rabbit 1.

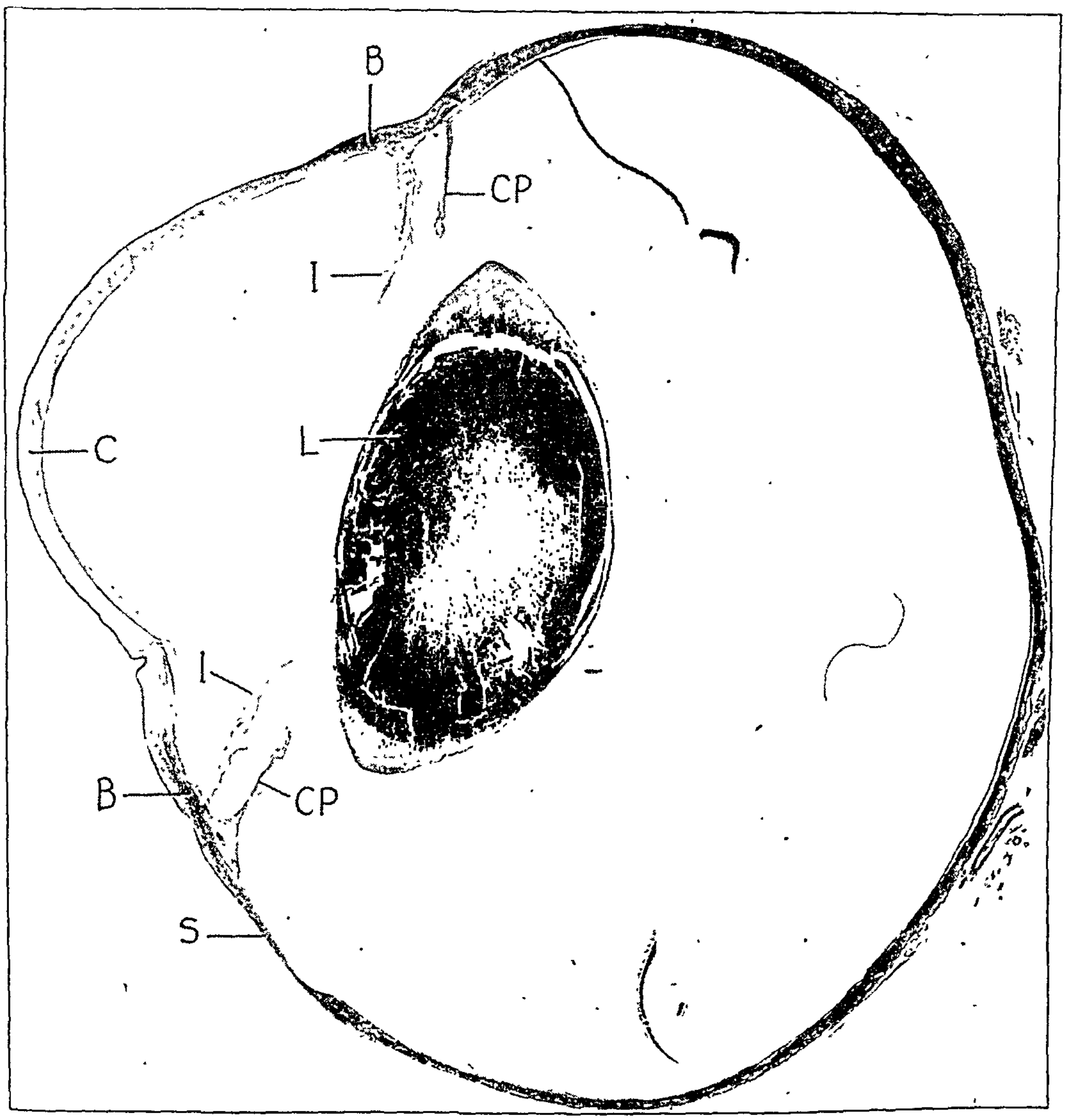

Fig. 29 (rabbit 1).—*B*, blood and pigment collected inside the sinus synechia; *CP*, atrophic ciliary processes, and *L*, lens.

It is my impression that with pure blood the dilation of the whole eyeball was greater than with defibrinated blood.

The late results of hypertension were clearly seen in rabbit 1 (fig. 29), which was killed twenty-three days after the injection. As in man, the iris and ciliary body became atrophic and receded backward. The sinus synechia thus became permanent. A new angle of the chamber was formed posteriorly. These retrograde changes were similar to those observed in patients with long-standing glaucoma.

COMMENT

If the changes produced by the injection of serum into the anterior chamber are compared with the reactions to defibrinated blood and pure blood, the first thing observed is that with serum hypertension started twenty-five minutes after the injection, while with defibrinated blood the increase of tension became manifest within ten minutes after the injection and remained at a high level during periods of from one hour to one day. In the rabbit in which serum was injected, as in the rabbits which received defibrinated blood, the intraocular tension increased even when no sinus synechia or true peripheral synechia had been developed. This was due to three factors.

1. The chemical composition of the aqueous became colloidal, the change considerably disturbing the absorption through the trabecular veins at the external wall of the sinus. This great increase in colloids in the aqueous produced an inversion of the normal current, the colloidal aqueous sucking fluid from the intrascleral vessels.

2. The filling of the sinus with serum or blood, and later with fibrin, mechanically prevented the normal aqueous in the anterior chamber from reaching the trabecular vessels on the surface of the sclera, the obstruction hindering the outflow of fluid and immediately promoting a great increase of intraocular tension.

3. The neurovascular response to hypertension was entirely different with serum than with blood. With serum the response was especially conspicuous in the iris, while with defibrinated blood the response was greater in the processes and base of the ciliary body. With the serum the iris underwent great vasodilation. This, in turn, increased the permeability of the walls of the veins and the capillaries, through which a larger amount of serum passed and infiltrated the stroma of the iris, which became thicker. The sinus was filled with serum and leukocytes. After two days the chamber became shallow. There was an endothelial reaction, with resulting attachment of the surface of the iris to the cornea and beginning production of a true anterior peripheral synechia.

With defibrinated blood the response was different. It was not limited to the iris but extended especially to the ciliary processes. These processes became edematous and swollen. The base of the ciliary body behind the processes also became edematous, increased in thickness and pushed the inner wall of the sinus outward, producing a mechanical closure of the cavity of the sinus. To this closure I have given the name "sinus synechia," as opposed to anterior peripheral synechia, which is produced by the adhesion of the surface of the root of the iris to the corneal limbus. The sinus synechia in animals corresponds to the anterior peripheral synechia in man, as in lower mammals the sinus is the principal channel for the outflow of the intraocular liquid. The sinus synechia usually did not develop until forty-eight hours after the injection. Later, the increased thickness of the root of the iris made the anterior chamber shallower, and the swollen processes pushed the root of the iris against the cornea. This entirely sealed the sinus and prevented the flow of aqueous into its cavity.

Besides this mechanical occlusion of the sinus, one must consider the action of the blood corpuscles, which act as a foreign body. They produce a greater neurovascular reaction than that to serum. Phagocytes migrate from the vessels in larger numbers and infiltrate all the structures around the sinus and fill its cavity. The endothelium then proliferates, as a result of irritation, producing bands of tissue which attach the root of the iris to the cornea, first temporarily and then permanently.

With pure blood conditions differed from those with defibrinated blood. The blood coagulated in the anterior chamber and the sinus, occluding the latter and coating the walls of the anterior chamber. Usually with pure blood hypertension lasted longer. The edema of the iris and the ciliary processes was greater, and the sinus synechia was already present at the end of twenty-four hours. The neurovascular response was more active than that with defibrinated blood. The whole blood, acting as a foreign body, produced an increase in the amount of liquid, made the anterior chamber deeper and so prevented the peripheral synechia from becoming wider. The endothelial reaction was also more intense, strands forming at the angle and around the clot in the chamber. The dilation of the cornea and the whole eyeball occurred earlier and was more pronounced.

Undoubtedly, chemical changes in the blood increased the irritation and led to the formation of lytic enzymes, which helped phagocytosis and the process of absorption of the blood. They have not been considered in this paper. The reader is referred to the work of Freund and Lustig,[11] Kikai and Riehm.

The responses elicited by injection of blood into the anterior chamber may be summarized as follows:

Mechanical.—When the angle is filled with blood, clot and fibrin, the aqueous is prevented from contact with the walls of the trabecular veins or the canal of Schlemm.

Physical.—The aqueous is laden with a large amount of proteins. These reverse the normal osmotic direction of fluid currents, attracting fluid from the vessels.

Chemical.—Chemical changes are produced in the blood injected into the anterior chamber by several reactions and ferments, e. g., by irritation and production of lytic substances.

Vital.—These include: 1. Sympathetic and parasympathetic stimulation, with dilation of the blood vessels, ophthalmotonic reaction and hypertension.

2. Neurovascular response, a defense reaction which produces dilation first of the vessels of the iris and then of the vessels in the ciliary body and the sclera, for the absorption of the excess of fluid and clearing of obstruction.

3. Increase in permeability of the walls of capillaries and veins.

4. Migration of leukocytes from the surface of the iris, the ciliary body and the scleral plexus for phagocytosis of foreign material.

5. Irritation of endothelial cells in the cornea and iris by proteins (?) and chemical substances.

6. Production of sinus synechia and peripheral synechia, first by contact and then by formation of fibrous connective tissue.

7. Great dilation of the eyeball in animals, similar to hydrophthalmos in children.

8. Retrograde changes, such as atrophy of the iris and ciliary processes and permanent peripheral synechiae.

CONCLUSIONS

Experiments made on rabbits, dogs and monkeys to observe the development of peripheral synechiae in conditions of increased intraocular tension show that the first step in the production of this increased tension was not the mechanical obstruction of the channels of outflow (cilioscleral sinus in lower mammals, trabecula and canal of Schlemm in monkeys) by the base of the ciliary body and the root of the iris, but a disturbance in the normal outflow of aqueous, which produced immediate hypertension. This, in turn, with the normal response of tissues by vasodilation and edema, produced a large swelling of the base of the ciliary body, which obliterated the cilioscleral sinus, with resulting adhesion (sinus synechia), and swelling of the processes. The thickened processes pushed the root of the iris forward, made the anterior chamber shallow and produced an anterior peripheral synechia.

The experiments consisted of injections of serum into the anterior chamber, as well as injections of pure and defibrinated blood, the use of substances foreign to the organism being avoided. Unfortunately, there is no other reliable method of producing experimental glaucoma.

Dr. Algernon B. Reese cooperated in the pathologic interpretation of the microscopic slides of the eyes operated on, and Dr. Edward Gallardo helped in the operations and the follow-up observations on the animals.

11. Freund, E., and Lustig, B.: Ueber die Muttersubstanz des im Blut und Muskel entstehenden Ammoniaks, Biochem. Ztschr. **240**:326, 1931.

APPRAISAL OF VALUE OF AN ORTHOPTIC CLINIC IN PRIVATE PRACTICE

E. C. ELLETT, M.D.; R. O. RYCHENER, M.D., AND
JEAN S. ROBINSON, B.A.
MEMPHIS, TENN.

The Memphis Orthoptic Clinic, available to all ophthalmologists in that city, has been in operation for the past ten years. It was organized in a frank spirit of skepticism; because of this feeling, its facilities have been available to patients without special reference to expense, this provision allowing the ophthalmologists of the city to refer to it patients with any type of muscular condition for treatment for as long as seems desirable. We have studied the records of the clinic to determine whether it has justified its existence.

In the last five years, 958 patients were seen at least once for examination and diagnosis, with a large number of whom members of the staff were able to maintain personal contact. Of the latter number, 345 were found suitable for orthoptic training and have come at varying periods for such training. For the past year, the two groups, the patients who remained under observation and those who received orthoptic training, numbered 389 and 334 respectively, the growth indicating a healthy increase, appreciation of what an orthoptic clinic can do for private patients. At present, the clinic has 53 patients who are given regular office treatment for half-hour periods, three times a week.

The clinic is operated by two trained technicians, of whom one (J.S.R.) is certified by the American Board of Orthoptic Technicians. If space and talent were available, the number of attendants could well be increased.

USEFUL INSTRUMENTS

For the first step in orthoptic work, which is the diagnosis of the state of muscular balance the screen test with prisms, made for near and for distant vision and for the cardinal fields, is of prime importance. For the testing of fusion ability and projection, the most necessary piece of equipment is one of the major amblyoscopes. These include the synoptophore, the synoptiscope and the orthoptoscope. Of these, the synoptophore is the instrument with which we are most familiar at our clinic. Its adaptability and the clear view of the patient's eyes that it affords make an instrument of this type invaluable in actual treatment, as well as necessary in diagnosis. In its favor is the fact that it is not automatic, so that fine adjustments are facilitated. It is by means of the major amblyoscope that abnormal retinal correspondence is most easily detected, and it is with this instrument only that patients with this defect are treated binocularly.

A simple hand stereoscope should always be available for the development of fusion amplitude and stereopsis. With many manifest conditions it is of no use, and under no circumstances should it be employed when abnormal retinal correspondence is suspected. However, in a high percentage of cases in which orthoptic treatment is required, a stereoscope will be of value for both office and home treatment.

The junior metronoscope, equipped with rotary prisms, is an instrument which we have found to have many uses. We recommend it particularly for persons requiring treatment at reading distance; however, it is adaptable to other needs. Patients with convergence insufficiency are quickly benefited by prism reading. When suppression is suspected or is known to be slight, the metronoscope is made more useful by the addition of a reading bar. In cases of insufficiency the metronoscope has a real diagnostic value.

In our clinic we also make use of the following apparatus:

1. The standard phorometer with Risley prisms, plus a Project-O-Chart, for determination of muscular balance.
2. The stereo-orthopter, an automatic instrument with lateral motion, excellent for development of fusion amplitude and for training of stereopsis.
3. The Maddox cheiroscope, used in cases of suppression and those in which binocular coordination is true but weak.
4. The kinetic stereoscope, designed for rotary movement and guided by hand.
5. The Remy separator, a simple, easily made hand device for use in many cases of lateral imbalance.
6. A reading bar of the simplest design, which is of distinct usefulness in many cases of binocular imbalance in which voluntary control is being taught.
7. A red and blue filter, which is useful in recession exercises with a light and in cases of suppression in connection with the tracing of red drawings.

When one begins the examination of a patient, one cannot foretell that the trouble is muscular, since the symptoms vary so much; the routine tests should therefore at least be of such extent that any gross error is soon detected. These tests ordinarily consist in determination of visual acuity for far and near vision, a quick test with the screen and parallax, a measure of the near point of convergence and an estimate of the

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muscular balance for 20 feet (6 meters) and 14 inches (36 cm.) with vertical prism or the Maddox rod. Usually correction of the refractive error, when that is indicated by the presence of faulty vision or symptoms, gives the desired relief. In cases of squint or of more than the normal amount of heterophoria, further tests of binocular vision, fusion ability and muscular strength (prism divergence and prism convergence) are made, and if the conditions seem to justify it, or if symptoms of asthenopia persist after a careful correction of the refractive error and wearing of the prescribed glasses, the patient is referred for further study in the orthoptic clinic. It would be easy to tax the resources of the clinic by sending more people there, but the plan we follow gives us a chance to estimate the need of such tests and saves the time of the clinic workers. In other words, we try not to call on the clinic for such information as we should properly and easily acquire with the equipment in the trial case, nor do we hope to have the clinic look after patients who need only proper refraction or some form of local or general medical treatment.

The role of orthoptics in the treatment of binocular incoordination is unique in that there is no substitute for the part that it plays. Just as refraction has its own place, so does orthoptic treatment. Realization that the miraculous cannot be accomplished by this comparatively simple procedure will lessen the disappointment of those whose expectations are too great.

We do not make extravagant claims concerning progress made in cases in which orthoptic treatment has been prescribed, but by cautious procedure we are gradually coming to more definite conclusions about the value of such treatment. Two quotations from recent articles agree with our own experience and conclusions. Linksz [1] stated:

> Orthoptics was rendered a poor service by those early enthusiasts who defined it as the nonoperative, as opposed to the operative treatment of squint. There is but one way of treating squint; namely, by the purposeful integration of a number of different procedures, of which surgery, while the most dramatic, is but one, and orthoptics is another.

Lancaster [2] reported:

> Orthoptics is not exercising of the ocular muscles; it is not even primarily a procedure designed to straighten the eyes. It is the teaching of a patient to use his two eyes together for comfortable binocular vision. The emphasis in such training is the teaching of a skill in the use of unskilled neuromuscular coördination. Orthoptics will be of much greater value to physicians and their patients when its function is re-evaluated; not as primarily concerned with anomalies of eye position, but as devoted to helping the patient learn comfortable binocular visual habits.

At first, our efforts in orthoptic therapeutics were directed entirely toward the correction of squint in young persons. We soon discovered that we could not expect improvement in coordination with exercises alone, but that it was necessary to correct refractive errors by glasses and gross deviations by surgical means before much effect from orthoptic training could be expected. In addition, amblyopia must first be combated by occlusion, and in our experience no technic of occlusion other than complete occlusion of the seeing eye over a period of months has ever given satisfactory results. We have many records of cases in which visual acuity in an amblyopic eye has increased from 6/60 to 6/6 and remained so after removal of the occluder. On the other hand, we have had many patients whose vision could not be improved beyond 6/15, although there was no apparent ophthalmoscopic reason for the absence of improvement. Unless visual acuity is improved to 6/12 or better, our experience indicates that the ultimate goal of normal position of the eyes and third degree fusion cannot be reached. An exception to complete occlusion is made in the case of an accommodative squint; in such a case the striping [3] or lacquering of one lens is often desirable in an effort to overcome suppression.

Outstanding in our records were 2 cases in which use of glasses was not indicated, since orthoptic training accomplished normal coordination of the eyes. The first case was one of convergence excess. H. W., a child aged 4 years, was a patient of Dr. J. B. Blue and Dr. J. B. Stanford, who have given us permission to report their case in detail. The child wore no glasses, no refractive error being found on examination with homatropine cycloplegia. Visual acuity was 6/7.5 in each eye. The patient could hold his eyes parallel for distant vision, but on fixation of any object within a range of 3 feet (90 cm.) his left eye converged about 35 degrees. Fortunately, he was aware of diplopia as soon as his eye turned in, and he would immediately make an effort to straighten it, but it was impossible to focus for near vision. The child was placed under a regimen of daily orthoptic training, and at the end of several months he was able to read, draw, and the like, with the eyes held straight. He has used the stereoscope at home since and will undoubtedly require continued supervised training at intervals for several years longer.

In the second case, that of M. T., a girl aged 4 years, one of us (R. O. R.) had performed a successful operation for alternating convergent squint of 50 prism diopters. Glasses were not worn because the total refractive error determined with atropine cycloplegia was only a + 0.50 D. sphere. Visual acuity was 6/6 in each eye. The eyes

1. Linksz, A.: Objectives of Orthoptic Examination and Treatment, Am. J. Ophth. **26**:552 (May) 1943.

2. Lancaster, J. E.: *Orthoptics*: Education in Binocular Skill, Am. J. Ophth. **26**:463 (May) 1943.

3. Lyle, K., and Jackson, S.: Practical Orthoptics in the Treatment of Squint, London, H. K. Lewis & Co., Ltd., 1937, p. 33.

remained in perfect position for eight months, when, after a fright during a tornado, there was immediate convergence, with development of convergent squint of nearly the original amount. The patient was then placed under a regimen of daily orthoptic treatments. The condition gradually improved, but she had alternately good and bad days. On bad days the deviation measured 38 prism diopters of esophoria and 2 prism diopters of left hyperphoria. On good days her eyes were perfectly straight. With regular treatment for a month, she was able to hold her eyes parallel for several days at a time and was sent home with a stereoscope and simple fusion cards. She has been checked at intervals, and for the past year has shown no tendency toward deviation from the normal (fig. 2).

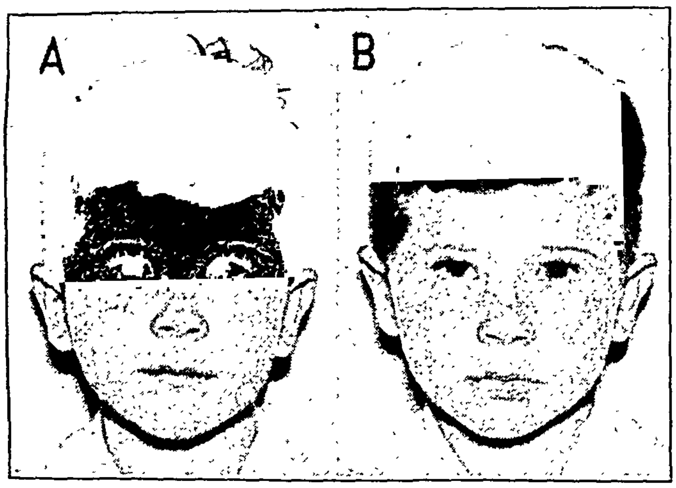

Fig. 1 (H. W.).—*A*, convergence excess prior to orthoptic training; *B*, result of orthoptic training.

ANOMALOUS RETINAL CORRESPONDENCE

Anomalous retinal correspondence, or false projection, is a difficult problem in the rehabilitation of patients with squint and is best handled by the trained orthoptic technician.

In the past five years, 36 per cent of the patients with squint examined in the orthoptic clinic had false projection. This agrees well with the reports of other workers, i. e., Davis,[4] 36 per cent; Pugh,[5] 50 per cent; Travers,[6] 50 to 60 per cent, and Hardy,[7] 60 per cent.

False projection has proved to be one of the greatest stumbling blocks in the training of true binocular coordination. The importance of detection of this condition when the original diagnosis is made cannot be emphasized too strongly. Neglect in taking note of anomalous correspondence amounts to emphasizing, instead of alleviating, the squint. The following cases serve to illustrate this statement:

CASE 1.—A. P. had alternating exophoria, with divergence excess. She reported fusion at 10 prism diopters of exophoria, but at this angle on the synoptophore or with correction by prisms there was definite shifting. She appeared to use an eccentric area of her right eye only in binocular vision, the fixation of each eye separately being true. Shifting was eliminated with a prism of 22 D., base in, and true fusion and stereopsis were finally obtained at this angle. If false projection had been ignored, exercises would have been given at the false angle, with the result that the squint would have become permanent. Instead, however, all exercises at first were given at what appeared to be the true angle until fusion was obtained. After fusion was well fixed at the true angle, adduction exercises were carried out, great care being given to observe that the patient did not revert to use of the old false area. When treatment was stopped, she had true fusion and stereopsis and held her eyes straight. Since the condition was divergence excess, much depended on the control she exerted when looking at distant objects.

CASE 2.—L. M. reported fusion at zero and at 10 D. of prism, base out. The true angle appeared to be 23 D. of prism, base out. The left eye projected falsely. Treatment was given at the true angle, and the lower half of the lens for the left eye was also occluded to prevent binocular vision for near vision but to encourage it for distant vision. It was not possible to say whether the patch was used correctly, but the results were fairly good. The final result was true fusion at 8 prism diopters of esophoria—the patient could overcome this and use the eyes held straight.

Fig. 2 (M. T.).—*A*, convergent squint prior to operation; *B*, result of operation and orthoptic training.

CASE 3.—F. L. reported fusion at 10 D. of prism, base out, but the child had definite exophoria. The true angle seemed to be 10 prism diopters of exophoria. Good fusion and stereopsis were developed at this angle. The eyes were held straight, and good convergence ability was acquired. If the fact that the subjective angle was false had not been taken into consideration, exophoria would have been emphasized, rather than overcome.

Particularly in operative cases we find that an abnormal retinal correspondence which has existed before operation is a handicap in post-

4. Davis, W. T.: Orthoptic Treatment of Strabismus, Tr. Am. Acad. Ophth. **41**:599, 1936.

5. Pugh, M.: Significance of False Projection in Squint, Arch. Ophth. **12**:459 (Sept.) 1934.

6. Travers, T. a'B.: Comparison Between the Visual Results Obtained by Various Methods Employed for the Treatment of Concomitant Strabismus, London, George Pulman & Sons, Ltd., 1936.

7. Hardy, L. H.: Orthoptics, Graduate Lecture read at the meeting of the American Academy of Ophthalmology, 1938.

operative treatment. The patient has a tendency to want to revert to his old habit, and much valuable time is lost at this strategic moment—immediately after operation. Theoretically and ideally, the most advisable procedure seems to be occlusion for development of macular fixation of the squinting eye and then operation, followed by treatment. This, for various reasons, is not possible in all cases.

We have the record of a patient (P. B.) whose case demonstrates what a handicap abnormal correspondence can be in postoperative training. He was an out-of-town patient and had been given no preoperative treatment. Immediately after operation he reported fusion on the synoptophore at 0 and 3 D. of prism base in. At this angle shifting was seen, and it appeared that his true angle was more nearly 10 D. of prism base out. He returned to his home within a few days, and there was no opportunity to give him any kind of binocular training. If this had been possible, however, treatment would have had to be given at his objective angle, in an attempt to develop true fusion. At this time, if it had not been for the falsely used area, abduction exercises would have been indicated. The outcome in a case of this kind is often a cosmetic, rather than a functional, improvement.

DIVERGENCE EXCESS

It is not possible to make a general statement concerning patients with divergence excess, since so much depends on the person. The tendency to diverge to excess for distance usually remains, but development of the ability to overcome this tendency is the purpose of orthoptic training. The factors of cooperation and mental effort on the part of the patient affect to a great extent the final result. Many such patients require operation, as well as orthoptic training.

The factor of mental effort is one which cannot be ignored in the successful treatment of any kind of binocular imbalance. Without the patient's full cooperation, and that cooperation includes a positive striving toward the goal as explained by the physician and kept in view by the technician, the achievement of the desired result will be hindered. This is true with patients of all ages.

The adult, who as a rule seeks relief from discomfort, should give his cooperation without question. Yet surprisingly often he has to be persuaded to do so. We believe the best method with adults is the full explanation of the common sense basis of the treatment. The sound logic of orthoptic training, coupled with its comparative ease and simplicity, should appeal to the average intelligent adult.

In the case of the teen age patient the cosmetic result is usually the point of attraction. With the small child the idea of showing what he can do seems to be the theme to stress. Some entertainment is necessary, and the child with imagination is the ideal patient. The method of reward, however wrong psychologically, must at times be resorted to. Much ground is gained when the person working with the child can secure his affection and esteem. It should be stressed that securing of this cooperation, by whatever means, is all-important with patients of all ages.

In our cases of retinal detachment, we have with impunity severed extraocular muscles in order to expose the proper scleral area, and in but few instances has there been any postoperative heterophoria. However, the report of a single case will illustrate the aid which the orthoptic clinic can give in the treatment of such complications.

A. D. M., a man aged 65, sustained an enormous tear and detachment of the retina in December 1937, for which diathermy operation was performed by one of us (R. O. R.) on Jan. 7, 1938. The left superior and external rectus muscles were reflected and then resutured to the stumps with fine chromic catgut. After recovery of normal vision, there were pronounced divergence and hypertropia of the left eye. On the synoptophore there were simultaneous macular perception, fusion and stereopsis at 24 D. of prism, base in, and left hypertropia of 7 to 18 prism diopters. Diplopia and vertigo were constant symptoms. Thirteen orthoptic treatments resulted in notable improvement in ocular measurements to 10 D. of prism, base in, with hyperphoria of 6 prism diopters. The patient later overcame this defect by constant effort and obtained fusion and stereopsis at zero. He has maintained this ability up to the present, with entire relief from his symptoms.

DIVERGENCE INSUFFICIENCY

Many patients with divergence insufficiency are made more comfortable when the power of prism divergence is built up. The clinic records the experience of many men who failed the preliminary Army aviation tests because of weakness in divergence power but who were enabled through proper exercises to qualify for the Air Forces. Similar results were experienced by laboratory technicians who had difficulty in the use of the binocular microscope and by patients with headaches and other symptoms of asthenopia for which no cause other than mild heterophoria could be discovered and who became perfectly comfortable after orthoptic training.

CONVERGENCE INSUFFICIENCY

In our experience the patients who have the best prognosis and respond most rapidly are those with convergence insufficiency. Treatment for alleviation of this condition is admittedly simple, but it does not follow that this deficiency is any less worthy of notice. Patients suffering

from lack of good convergence ability feel real discomfort which, though not disfiguring or serious, can hamper them considerably in their work. Sometimes the symptoms are experienced only with close work, whereas, again, discomfort is felt rather generally with use of the eyes at any distance. Training of a better and easier convergence habit at the office, supplemented by home exercise, is the usual procedure. Many out-of-town patients with this condition are seen. Happily for them, successful treatment can be directed at home. Of course, as is the case in any kind of training process, much depends on the amount of effort put forth by the patient. It is true, however, that more can be done for himself by a patient needing exercises for convergence insufficiency than can be done by a patient with any other condition. It is probable that there are physicians who disparage treatment for convergence insufficiency, dismissing the sufferer with a half-hearted suggestion concerning finger to nose convergence exercises. There are also persons with convergence weakness who are advised simply not to use their eyes for much close work, and who inevitably become dissatisfied patients. We feel it urgent to bring these possibilities to mind, since in our experience many patients with this condition, who are uncomfortable, although they have had proper refraction, are completely relieved by orthoptic training.

TRUE AND LATENT CONVERGENCE INSUFFICIENCY

In this field, we should like to differentiate between true convergence insufficiency, in which the diagnosis is apparent because of a marked recession of the convergence near point, a high degree of exophoria for near vision or a frank disparagement in the normal 3 : 1 or 4 : 1 relation of prism convergence to prism divergence, as measured on the phorometer, and a latent or hidden tendency to convergence insufficiency, as demonstrated by normal phorometric measurements accompanied by a history of ocular discomfort on close use of the eyes. The latter we believe to be the condition of a large group of patients who make the rounds of various ophthalmologists and who are usually thought to be victims of neurasthenia or hysteria. Careful checking with the phorometer may disclose a slight weakness in prism convergence, but usually the measurements of the muscle strength are within normal limits. However, examination with the junior metronoscope, equipped with rotary prisms, will invariably disclose a poor reading ratio, i. e., the relation of prism convergence to prism divergence, which should be at least 2 : 1, and preferably 3 : 1 or 4 : 1. On this instrument are simulated the fixations and regressions which are a part of the normal reading habit. Measurements of the vergences under the stress of movement of the eyes from left to right, as in reading, give a true estimate of muscle-power in ocular activity, as compared with the static measurement of unmoving eyes examined on the phorometer by fixation of a single point object. Since acquainting ourselves with the value of prism reading tests for such patients, we have looked more closely for the latent convergence insufficiencies and find that they occur more frequently in our practice than we would have believed possible.

The diagnosis of convergence insufficiency is often easy—the existence of a condition of greater exophoria for near than for distant vision, together with a poor convergence near point. However, there is no definite rule which can be set up concerning exact measurements that leads to a diagnosis of this difficulty. First, symptoms vary greatly—from headaches, double vision, tired eyes and burning lids to dizziness and actual unsteadiness in walking. We have found many combinations of symptoms, as well as many different groupings of indicative measurements. There sometimes exists a decided exophoria for near vision with a good convergence near point. At other times there may be a poor convergence near point with a normal physiologic exophoria. Either of these combinations of measurements may be present with good or poor prism vergences.

There is, however, a significant finding that in our experience consistently indicates the need for convergence training at the near point. This measurement is called the reading ratio. It is the ratio of prism divergence to prism convergence at the near point during actual reading, which involves the changing of fixation, as is done normally during reading or during use of the eyes in almost any other occupation. In a few instances this measurement has been the only indication of the difficulty present. In other cases it has been a deciding factor in the course of treatment. In all cases it has borne out the testimony of other positive diagnostic measurements.

There may be several ways of setting up means of taking a reading ratio, but the method we have found most satisfactory is the use of a table model of the junior metronoscope. This is an instrument equipped with reading rolls lighted from within and with an automatic shutter arrangement whereby fixation is necessarily changed in order to read the complete line. There is also firmly attached a set of rotary prisms at reading distance, complete with head rest. The patient places his head firmly against the rest

with his eyes close to the prisms. The reading correction is worn. As the prisms are turned base in and base out to find the breaking point, the patient changes his fixation as he reads across the line, guided by the opening and closing of the shutters. The resulting ratio is one prism of divergence to prism convergence—a relation made more significant in the case of convergence insufficiency, since the patient is actually doing the thing with which he has trouble while the measurement is being made. We find the same relation between prism divergence and prism convergence is necessary for comfort in reading as for distance vision.

It can easily be seen that by means of the same instrument, the metronoscope, the training of better convergence can be effectively given and the diagnosis of convergence deficiency made. We depend to a great extent on this instrument for the treatment of persons with this weakness. Other methods include the use of the synoptophore, the stero-orthopter and the Remy separator.

In the past five years the clinic has had 453 patients with convergence insufficiency, 148 of whom, or 33 per cent, would be classified as having latent convergence insufficiency. Of 136 patients with convergence insufficiency treated in the clinic, 52, or 38 per cent, would be said to have the latent form. Of the 136 patients treated, 125 felt their trouble was definitely improved. Of the 11 for whom no improvement was recorded, 5 dropped out and did not complete the treatment. The remaining 6 patients had other conditions, such as allergy and migraine, which were partly responsible for the symptoms for which they sought relief.

Ninety-one persons with convergence insufficiency were given home treatment, consisting mainly of the use of a stereoscope and delta "base out" cards. Simple fusion cards made at the office were given children for home use. Other training included the use of loose prisms base out, finger to nose convergence exercises and voluntary convergence exercises [8] with finger and distant object. (The subject fixes on the finger at a near point, being conscious of a double distant object; the finger is then removed, and the patient tries to keep the image of the distant object doubled by looking at an imaginary near point.)

CONCLUSION

We have found the Memphis Orthoptic Clinic a valuable adjunct in the handling of our private patients, and we expect to profit by its continued aid in the future.

1720 Exchange Building.
1720 Exchange Building.
720 Exchange Building.

8. Lyle and Jackson,[3] p. 153.

DRUSEN OF THE OPTIC NERVE SIMULATING CEREBRAL TUMOR

NATHAN S. SCHLEZINGER, M.D.; JOSEPH WALDMAN, M.D., AND
BERNARD J. ALPERS, M.D.
PHILADELPHIA

Drusen of the optic nerve constitute a characteristic ophthalmologic disorder, which was first described in 1858 by Müller.[1] In addition to the term drusen, the same condition has been referred to by various authors as "hyaline bodies," *Drusenbildungen* and *Kalkdrusen*. A review of the literature discloses that the occurrence of drusen of the optic nerve without symptoms is well known. Some authors have pointed out the association of drusen of the optic nerve with ophthalmologic diseases, such as retinitis pigmentosa, glaucoma and melanosarcoma. Several have noted the relatively frequent concurrence of drusen of the optic nerve with disorders of the nervous system.

Our attention was recently directed to this interesting neuro-ophthalmologic disorder by the observation of 2 patients who demonstrated that drusen of the optic nerve may in some instances be characterized by clinical features closely resembling those of tumor of the brain. Although pneumoencephalographic study may be necessary in order to establish definitely the correct diagnosis, we wish to call attention to cases of this type because the outlook and management are so different from the prognosis and treatment of tumors of the brain.

REPORT OF CASES

CASE 1.—*Right hemicrania for years; left-sided headaches for three years. Drusen of the optic nerve, with slight elevation of the disk. Results of neurologic examination negative; pneumoencephalogram negative for cerebral tumor.*

History.—J. M., a woman aged 23, a woolen mill worker, was admitted to the neurologic service of the Jefferson Medical School Hospital on March 19, 1940, complaining of headache for three years. Her father had been subject to convulsive seizures, and the mother had migraine; the family history was otherwise without interest from a neurologic standpoint. The past history revealed the occurrence of typical hemicrania as long as the patient could remember, the free interval between headaches varying from four to six weeks. The headaches were on the right side; they usually appeared prior to the menstrual period, were characterized by prodromal paresthesias involving the face, tongue anc arm homolaterally and were associated with vomiting and with amblyopia involving the right eye. Except foi the typical attacks of migraine, the patient had been ir good health until about three years before admissioı to the hospital, when the right *hemicrania* was gradu ally replaced by headaches in the left parieto-occipita region, associated with pain in the left eye. These head aches were relieved temporarily by the wearing o glasses, but they soon recurred and became progressivel more frequent and more intense. In the months pre ceding admission the headache was present daily an often awoke the patient during the night. Tinnitus an transient vertigo were noted for several weeks preced ing admission. There were no other symptoms referabl to the nervous system.

Physical Examination.—The patient was well devel oped. A scar on the right side of the neck was th result of removal of a cyst ten years before. The hear lungs and abdomen were grossly normal. The bloo pressure was 120 systolic and 70 diastolic.

Neurologic Examination.—Station and gait were nor mal. There was a fine tremor of the eyelids and c the fingers on extension. No evidence of ataxia o incoordination was noted. The motor power was we preserved everywhere. The tendon reflexes were equa and active everywhere except for a relatively hyper active patellar reflex on the left side. The abdomin reflexes were active and equal on the two sides. Ther were no pathologic reflexes. Pain, position and vibratio senses were intact. There was slight facial asymmetr but no true weakness of the face, palate or tongu Neuro-ophthalmologic examination showed relati prominence of the right eye, verified by the exophtha mometer (right eye, 22 mm. and left eye, 15 mm.). Tł pupils were round, regular and equal and reacted we to light and in accommodation. The extraocular mov ments were normal. The corneal reflexes were equal active on the two sides. Examination of the fund disclosed many lemon yellow drusen on and near tl upper and nasal margins of the optic disk bilaterall The borders of the nerve head elsewhere were free drusen and appeared striated and somewhat gray. Tl optic disks appeared elevated, but the degree of elev tion could not be measured. The physiologic cup w present but small. The ratio of vessels was norm The macular area was normal.

Laboratory Studies.—The results of urinalysis and tl blood count were within normal limits. The sugar the blood measured 91 mg. and the nonprotein nitrog 39 mg. per hundred cubic centimeters. The Wasse mann reactions of the blood and the spinal fluid we negative. The cerebrospinal fluid showed an initi pressure of 165 mm., contained less than 1 cell per cub millimeter and had a total protein content of 12 m per hundred cubic centimeters. The electrocardiogra was normal. The basal metabolic rate was + 1 per ce Roentgenographic examination of the skull, includi special views of the sella turcica, the orbits and tl

From the Department of Neurology, Jefferson Medical College of Philadelphia.

Read at a meeting of the College of Physicians of Philadelphia, Section on Ophthalmology, Oct. 21, 1943.

1. Müller, H.: Anatomische Beiträge zur Ophthalmologie, Arch. f. Ophth. 4 (pt. 2):1, 1858.

optic foramens, revealed nothing abnormal. An encephalographic study on March 26 showed a well outlined ventricular system, which was symmetric and showed no displacement or filling defects (fig. 1).

CASE 2.—*Frontal headaches for one and a half years; nausea and vomiting. Drusen of optic nerves, with 1 to 1.5 D. of papilledema bilaterally; constriction of visual fields and enlargement of blindspots. Results of neurologic examination negative; pneumoencephalogram negative for cerebral tumor.*

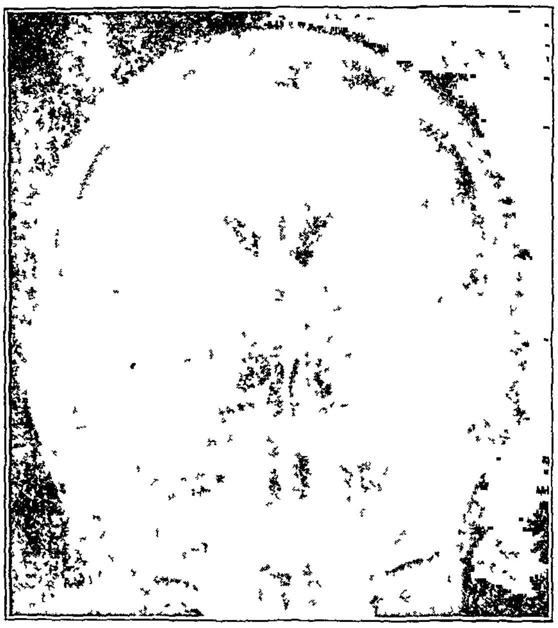

Fig. 1 (case 1).—Encephalogram, showing a symmetric ventricular system, with no displacement or filling defects.

History.—F. C., a motorman aged 35, was admitted to the neurologic service of the Jefferson Hospital on Jan 28, 1942, complaining of headaches for the past one and a half years and of vomiting for the past two years. One brother had committed suicide; the mother, the sister and a nephew were known to have had cystic nodules over various parts of the body; the family history was otherwise without significance from a neurologic standpoint. The past history included a tonsillectomy at 10 years of age and an appendectomy at 20 years of age. While he was working in a coal mine, at the age of 17, the patient sustained an injury to his left leg, which was not severe. Cystic nodules had been removed from behind the left ear and the left elbow. Except for these episodes the patient had apparently been in good health until the onset of his present difficulty, which developed gradually early in 1940.

At this time vomiting began, as often as two or three times a day, usually, but not always, accompanied by nausea. During the summer of 1940 frontal headaches appeared, dull in character and lasting three or four hours. These attacks occurred three or four times a week at first, but they became more intense and more frequent until they were almost constant by the summer of 1941. The vomiting persisted unchanged until November 1941, but after this it was observed on only four or five occasions. The headaches occurred without change until his admission to the hospital. The patient had noted increased fatigability and some unsteadiness of gait at times prior to entrance.

Physical Examination.—The patient was fairly well developed. There was evidence of pronounced lymphoid hyperplasia in the pharynx. The heart, lungs and abdomen were grossly normal. The blood pressure was 120 systolic and 80 diastolic. There was a post-traumatic scar on the left leg.

Neurologic Examination.—Station and gait were within normal limits. There was no evidence of ataxia or incoordination. The tendon reflexes were equal and active except for an inconstant, relatively hyperactive biceps reflex on the left side. The abdominal reflexes were active. The plantar reflex was not pathologic. Pain, position and vibration senses were intact. The pupils were round, regular and equal and reacted well to light and in accommodation. The extraocular movements were normal. The corneal reflexes were active. There was no weakness of the face, palate or tongue. Neuro-ophthalmologic examination showed the following abnormalities in the fundus bilaterally (fig. 2): The temporal and superior portions of the optic disk had a dirty gray pallor; the cup was small, and the lamina cribrosa was not seen. Characteristic drusen, lemon yellow in color, were scattered throughout the nerve tissue of the optic disk. The superior and nasal margins of the optic disk were indistinct and elevated to a level between 1 and 1.5 D. The appearance of the retinal vessels was normal, and there were no retinal exudates or hemorrhages. Visual acuity without correction was 20/20 in the right eye and 20/30 in the left eye. Examination of the visual fields (fig. 3) showed slight peripheral constriction and slight enlargement of the blindspot bilaterally.

Laboratory Studies.—The blood count and the results of urinalysis were within normal limits. The sugar of the blood measured 79 mg. and the nonprotein nitrogen 30 mg. per hundred cubic centimeters. The Wassermann reactions of the blood and the spinal fluid were negative. The cerebrospinal fluid had an initial pressure of 170 mm., contained less than 1 cell per cubic millimeter

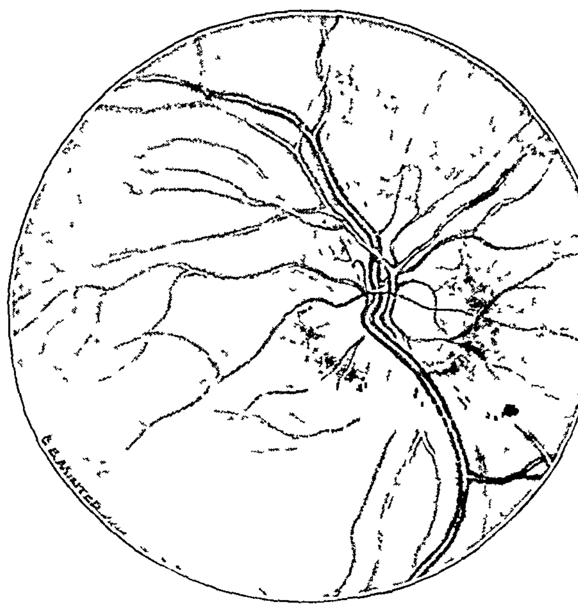

Fig. 2 (case 2).—Fundus of the right eye, showing characteristic drusen and an indistinctly outlined optic disk, with measurable elevation.

and had a total protein content of 24 mg. per hundred cubic centimeters and a normal colloidal gold curve. Laryngologic examination and biopsy of tissues from the nasopharynx confirmed the clinical impression of marked lymphoid hyperplasia of the pharynx. Roentgenographic examination of the skull, including special

views of the base and sinuses, revealed nothing abnormal. An audiometric test showed no significant impairment of hearing. The Bárány test revealed changes suggestive of multiple lesions involving the brain stem, together with absence of shock reaction. An electroencephalogram revealed normal cerebral potentials except for showers of sharp and slow wave formations in

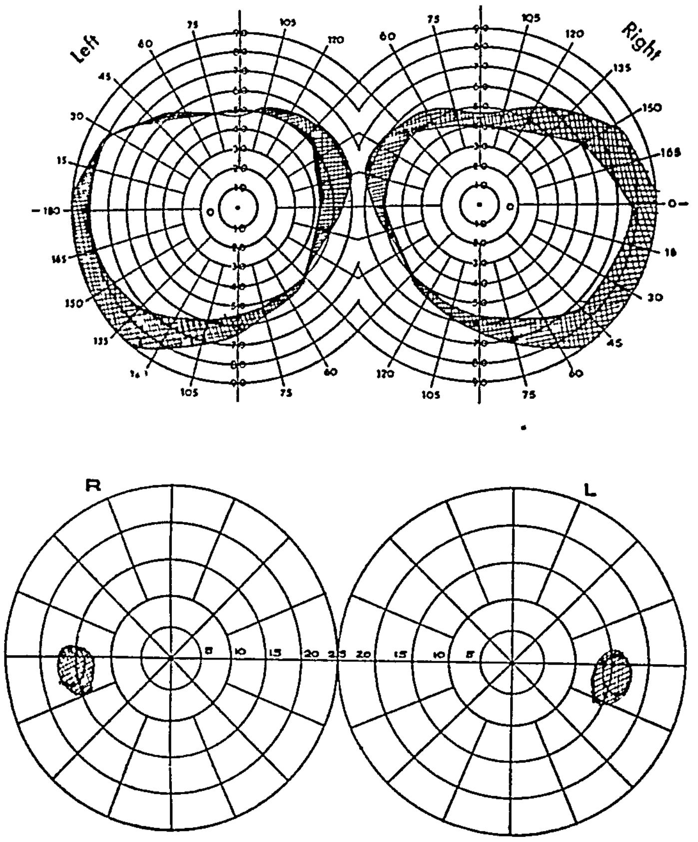

Fig. 3 (case 2).—Visual fields, showing slight peripheral constriction and slight enlargement of the blindspot bilaterally.

the left frontal and parietal areas, the significance of which was doubtful. Encephalographic examination, performed on February 7, disclosed (fig. 4) that the ventricles were well filled with air and were symmetric and normal in size and shape. The third and fourth ventricles were well shown and appeared normal. There was air in the basal cisterns and in the subarachnoid pathways.

After this procedure, the symptoms present on admission disappeared, and at the time of discharge the patient was asymptomatic.

The anamnestic data in these cases reveal a clinical syndrome chiefly characterized by headache, vomiting and an altered appearance of the optic disks somewhat suggestive of early papilledema. Therefore it is not surprising that the diagnostic possibility of cerebral tumor was seriously considered in both cases. This was true in spite of the fact that the drusen were detected in the optic nerves by the neurologist and the ophthalmologist. The conspicuous headache and vomiting, as well as such minor symptoms as vertigo, were believed to be sufficient to warrant an intensive search for the presence of cerebral tumor.

In case 1 the possibility of a close relation between the existing headaches and the past history of typical migraine was not overlooked. But such a relation was rejected because the patient's recent headaches differed so considerably from her previous migraine headaches. In case 2 there was no past history of headaches; the patient showed definitely measurable elevation of the optic disks, a slight peripheral constriction of the visual fields and enlargement of the blindspots.

No evidence of increased intracranial pressure was demonstrable by lumbar puncture in these cases. Routine chemical examination of the spinal fluid showed no abnormalities. Pneumoencephalographic studies in both cases disclosed no evidence of tumor of the brain, and the results were considered to be within normal limits. The results of our study in these 2 cases made evident the fact that the symptoms were not due to tumor of the brain. This conclusion directed our attention to the problem of correlating with drusen of the optic nerve the clinical syndrome which commonly is associated with cerebral tumor.

In 2 cases reported by Reese [2] the symptoms and signs were strikingly similar to those observed in our cases, and the presence of tumor of the brain was similarly suspected. In this connection it is interesting to observe that in both our cases there was a history of removal of cystic masses from the various parts of the body and that in case 2 there was a history of similar cysts affecting several persons of the same family. This may tend to support the

Fig. 4 (case 2).—Normal encephalogram.

hypothesis offered by Reese [2] in which drusen are considered to be *formes frustes* of tuberous sclerosis. The latter condition, in turn, was classified with conditions such as multiple neuro-

2. Reese, A. B.: Relation of Drusen of the Optic Nerve to Tuberous Sclerosis, Arch. Ophth. **24:**187 (July) 1940.

fibromatosis, Hippel-Lindau disease and the Sturge-Weber syndrome by van der Hoeve,[3] who suggested the term "phakomatoses" for all.

COMMENT

In order to evaluate the clinical significance of drusen of the optic nerve, this neuro-ophthalmologic disorder should be considered from a variety of standpoints. Since the time of the first report by Müller,[1] various suggestions as to the cause and pathogenesis of this condition have been offered. Predisposition was the etiologic factor favored in the report of Ancke,[4] Lauber,[5] Braun[6] and Leimgruber,[7] in which familial incidence was a conspicuous feature. Advanced age as an etiologic factor was suggested by Terson[8] but was disproved by Walker's[9] report of drusen in a 9 year old boy and by Gifford's[10] case of the lesion in an 11 year old girl. The age of onset is obscure in all cases, since the drusen are discovered incidentally in examination of the fundus. Sex was demonstrated to be an unimportant factor in the series reported on by Höeg,[11] in which 30 patients were females and 23 males. Toxic or infectious etiologic factors are conspicuously absent in the vast majority of cases; Lauber[5] reported a case in a man with alcohol-tobacco amblyopia. Cirincione[12] showed that drusen of the optic nerve do not have the same origin as drusen of the choroid. Iwanoff[13] expressed the belief that drusen were colloid bodies. Oeller[14] disagreed with this concept and suggested that drusen originated as droplets of myelin. Coats[15] favored the origin from "small homogeneous droplets of hyalin." Lauber stated that misplaced pigment epithelium was the probable site of origin. Parsons[16] offered the theory of origin from antecedent exudates in the nerve head. Fuchs[17] favored the origin from neuroglia, and this theory was also supported by Collins and Mayou.[18] Corrado[19] postulated that the source of drusen was in the nature of "heterotopic calcinoses," due to parathyroid dysfunction. Reese[2] offered the hypothesis that drusen are *formes frustes* of tuberous sclerosis.

The preponderance of evidence supports the belief expressed by Fuchs[17] that drusen are derived from the neuroglia cells in the optic nerve, probably as a result of some local irritative process, although either metabolic or degenerative processes are possible. Therefore, whatever the ultimate origin, it is likely that drusen start as minute globules of hyalin, which increase in size by accretions in layers or by fusion. Hyalin deposits in the neuroglia were observed by Goldstein and Givner.[20] Tobler,[21] in a comprehensive treatise, described the results of a series of chemical analyses. He concluded that drusen were composed of a split product of albumin which is similar to hyalin, and which has a tendency to take up calcium.

Samuels[22] strongly favored Fuchs's hypothesis that drusen arise from abnormal secretions of hyalin by proliferative neuroglia cells in the papilla. Hirschberg and Cirincione[23] proved that

3. van der Hoeve, J.: Eye Symptoms in Phakomatoses, Tr. Ophth. Soc. U. Kingdom **52**:389, 1932.

4. Ancke, R.: Beiträge zur Kenntnis von der Retinitis pigmentosa, Centralbl. f. prakt. Augenh. **9**:167, 1885.

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6. Braun, W.: Ueber familiäres Vorkommen von Drusen der Papille, Klin. Monatsbl. f. Augenh. **94**:734, 1935.

7. Leimgruber, M.: Erbforschungen über die Drusen der Sehnervenpapille, Arch. f. Ophth. **136**:364, 1936.

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9. Walker, C. H.: A Case of Hyaline Bodies at the Optic Disk, Tr. Ophth. Soc. U. Kingdom **35**:366, 1915.

10. Gifford, H.: An Unusual Case of Hyaline Bodies in the Optic Nerve, Arch. Ophth. **24**:395, 1895.

11. Höeg, N.: Ueber Drusen im Sehnervenkopf, Arch. f. Ophth. **69**:355, 1908.

12. Cirincione, C.: Concrezioni nella testa del nervo ottico, Clin. ocul. **5**:1599, 1904.

13. Iwanoff, A.: Ueber Neuritis optica, Klin. Monatsbl. f. Augenh. **6**:421, 1868.

14. Oeller, J. N.: Beiträge zur Lehre von der Chorioretinitis pigmentosa, Arch. f. Augenh. **8**:435, 1879.

15. Coats, G.: Concretions in the Papilla and Corpora Amylacea in the Retina, Tr. Ophth. Soc. U. Kingdom **32**:119, 1912.

16. Parsons, J. H.: Hyaline Bodies at the Optic Disc, Tr. Ophth. Soc. U. Kingdom **23**:136, 1903.

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19. Corrado, M.: Sulla patogenesi della concrezioni calcarie della papilla in rapporto ai processi di calcinosi, Ann. di ottal. e clin. ocul. **62**:721, 1934.

20. Goldstein, I., and Givner, I.: Calcified Hyaline Deposits (Drusen) in the Optic Disk, Arch. Ophth. **10**:76 (July) 1933.

21. Tobler, T.: Ueber Kalkdrusen in der Papille des Nervus opticus und über Kombination derselben mit zystoider Entartung der Macula lutea, Ztschr. f. Augenh. **47**:215, 1922.

22. Samuels, B.: Drusen of the Optic Papilla, Arch. Ophth. **25**:412 (March) 1941.

23. Hirschberg, J., and Cirincione, G.: Ueber Drusen im Sehnervenkopf, Zentralbl. f. prakt. Augenh. **15**:166 1891.

drusen were not amyloid in composition, and they described the evolution of a gas when the hyalin bodies were treated with hydrochloric acid.

Clinicopathologic descriptions have been made by Hirschberg and Cirincione,[23] Gurwitsch,[24] de Schweinitz,[25] Sachsalber,[26] Cirincione,[12] Coats [15] and Lauber.[5] In two recent reports by Reese [2] and Samuels,[22] the results of careful pathologic study of eyes containing drusen of the optic nerve have been recorded. Reese [2] stated that the incidence of drusen over a 7 year period in routine microscopic examinations of eyes removed for various causes was 1 per cent of a series of 893 globes. Histopathologic study of eyes containing drusen of the optic nerve discloses that the lesions are usually situated on the nasal side and, with rare exceptions, anterior to the lamina cribrosa. According to Samuels,[22] an especially frequent location for drusen is on the nasal side, in the recess between the scleral spur and the lamina cribrosa. The lesions consist of a variable number of discrete nodules or of a conglomeration of partially fused nodular masses, which have a concentrically laminated structure. A large conglomerate mass is characteristically associated with smaller satellite lesions. The bulb of the lesion is composed of an amorphous, hyalin substance, which not infrequently shows evidence of calcification. These nodular masses are not encapsulated and thus differ definitely from corpora amylacea; the latter also are distinguished by the fact that they show no lamellation. Drusen are differentiated from corpora aranacea by the fact that the latter are always situated behind the lamina cribrosa, are usually calcified and are closely related to the dura or the arachnoid.

In the earliest stage of development drusen of the optic nerve appear as pale yellow, glistening points in the optic disk, usually near the edges. It is at this stage that the diagnosis is uncertain, especially when there is a coexisting ocular ailment. The nasal side of the papilla seems to be the area most frequently affected. This side is also the site of predilection for glial membranes, which is in keeping with the fact that the papilla is thicker on the nasal side, with, consequently, more glial tissue present there. In the later stages of development, the diagnosis becomes more certain as the drusen assume their more typical appearance in the form of round, discretely grouped or conglomerate, partially fused nodular masses, which are gray-white or blue-white. The drusen tend to become increasingly massed near the edge of the disk, although they are sometimes scattered throughout.

The appearance of drusen on examination of the fundus varies with the depth of the lesion. The drusen which are situated anterior to the choroidal ring are easily recognizable and present a striking ophthalmoscopic picture. They may reflect the light with much brilliance, appearing as shining white or pale lemon yellow bodies, with beadlike contour. They have been described in picturesque terms as resembling a shower of gold coins, a cluster of grapes, a mass of frog eggs or tapioca grains. They are more or less translucent. As a lobulated mass they may completely cover the optic disk, which may be swollen. An increase in elevation as high as 14 D. has been reported. In addition to the possible elevation, there may be an increase in diameter of the papilla, due to extension into the surrounding retina. The drusen may be either anterior or posterior to the retinal blood vessels, and occasionally a mass of these bodies may completely hide the vessels at some point in their course. It is doubtful whether calcification of the lesion can be distinguished by means of the ophthalmoscope.

The drusen which are situated deep in the sclerochoroidal canal are probably not visualized with the ophthalmoscope because of the overlying cover of nerve fibers and capillaries. These drusen are especially important to bear in mind clinically, since they may produce an abnormal fulness of the papilla, which may be accompanied by enlargement of the blindspot. In many instances, so-called pseudoneuritis may really represent unsuspected, deeply situated drusen. In such cases the possible confusion with early papilledema is obvious.

In most cases observation of the condition over a considerable period shows little or no change in the ophthalmoscopic appearance which would indicate progression. However, in his report of a case of a 9 year old boy, Walker [8] described a progressive increase in the size and number of drusen over a period of four years. Lauber,[5] similarly, observed, in the case of a woman, a notable increase in drusen over a period of fifteen years. Reese [2] also noted growth over a period of two years in a 17 year old youth.

The occurrence of drusen of the optic nerve in association with a variety of local ocular disorders has been described by many authors. The concurrence with retinitis pigmentosa was noted by Müller,[1] Nieden,[27] Oeller,[14] Tillé and Tran-

24. Gurwitsch, M.: Ueber hyaline Bildungen im Sehnervenkopfe und in der Netzhaut bei Morbus Brightii, Zentralbl. f. prakt. Augenh. **15**:225, 1891.

25. de Schweinitz, G. E.: Hyaline Bodies (Drusen) in the Nervehead, Tr. Am. Ophth. Soc. **6**:349, 1892.

26. Sachsalber, A.: Beitrag zur Drusenbildung im Sehnervenkopfe, Beitr. z. Augenh. **3**:1, 1898.

27. Nieden, A.: Ueber Drusenbildung in und um den Optikus, Arch. f. Augenh. **20**:72, 1889.

tas,[28] McKenzie,[29] Remak,[30] Ancke,[4] Morton and Parsons,[31] Walker,[9] Topolanski[32] and Masselon.[33] The coexistence of drusen with melanotic sarcoma was observed by Coats[15] and Cibis.[34] Drusen in conjunction with chorioretinitis was reported by Chevallereau,[35] Juler,[36] Lawson[37] and Löhlein.[38] The association with glaucoma was recorded by Demaria,[39] Athens[40] and Samuels.[22]

Various neurologic disorders have been observed in conjunction with drusen of the optic nerve. Facial nerve paralysis was noted by Hirschberg and Cirincione,[23] and death due to cerebral hemorrhage, by Hirschberg and Birnbacher.[41] Chronic hydrocephalus caused death in the case reported by Wedl and Bock.[42] Hypophysial tumors were present in cases reported by Lauber[5] and Rath.[43] Nieden[44] described 2 cases in which there had been a history of head injury, while de Schweinitz[25] noted that his patient had been shot in the head. Fejér[45] reported on a patient with bilateral paresis of the oculomotor nerve who was also suspected of having tumor of the brain. Meningomyelitis and optic neuritis occurred in a case described by Stood.[46] Neurasthenia was a noteworthy feature in patients reported by Nieden[27] and Coats.[15] Amaurosis and insanity were observed in 1 case by Iwanoff.[13] Mendel[47] noted hysteria and chlorosis in his patient.

In the vast majority of cases of drusen of the optic nerve there is no impairment of vision. Asymptomatic cases with negative anamneses have been described by Nieden,[27] Lauber[5] and Höeg.[11] It is amazing in some instances to note the disproportionately mild effect on vision of what is so often an apparently massive change in the optic disk. This is explained by the histopathologic observation that the optic nerve fibers may be twisted in their course by the drusen but remain normal in caliber. However, there appears to be no doubt that drusen of the optic nerve, in a relatively few cases, may lead to severe impairment of vision. Such cases have been reported by Iwanoff,[13] de Schweinitz,[25] Cirincione,[12] Fejér,[45] Wedl and Bock,[42] Lauber,[5] Rabitsch[48] and Shumway.[49] A patient was observed by Nieden[27] over a period of years, during which exacerbations and remissions in visual impairment were directly correlated with the phasic manner of growth of the drusen. These more serious effects of drusen are probably a result of compression of the optic nerve fibers in the instances in which the drusen are situated in the sclerochoroidal canal.

The usually mild alterations in the visual fields, such as slight enlargement of the blindspot with or without nonspecific peripheral constriction, are directly attributable to the presence of drusen when a coexisting ocular condition has been excluded. Contraction of the visual fields has been reported in such cases by Stood,[46] Nieden,[27] de Schweinitz,[25] Streiff,[50] Rabitsch,[48] Lauber,[5]

28. Tillé, H., and Trantas, N.: Verrucosités hyalines, prépapillaires (drussen) chez un homme jeune atteint de rétinite pigmentaire, Bull. Soc. d'opht. de Paris, April 1934, p. 243.

29. McKenzie, G. W.: Drusen of the Optic Nerve, Retinitis Pigmentosa, and Vitreous Opacities, Eye, Ear, Nose & Throat Monthly **13**:293, 1934.

30. Remak: Ein Fall von excessiver Drusenbildung in der Papille bei atypischer Retinitis pigmentosa, Zentralbl. f. prakt. Augenh. **9**:257, 1885.

31. Morton, A. S., and Parsons, J. H.: Hyaline Bodies (Drusenbildung) at the Optic Disc, Tr. Ophth. Soc. U. Kingdom **23**:135, 1903.

32. Topolanski, A.: Drusen am Sehnerveneintritt und Pigmentdegeneration der Retina, Ztschr. f. Augenh. **20**:584, 1908.

33. Masselon, J.: Infiltration vitréuse de la retine et de la papille, Bull. et mém. Soc. franç. d'opht. **2**:1, 1884.

34. Cibis, P.: Zur Klinik und Anatomie der Drusenbildung in der Papille und über Kombination derselben mit einem Melanosarkom der Aderhaut, Klin. Monatsbl. f. Augenh. **105**:78, 1940.

35. Chevallereau, M.: Verrucosités hyalines du nerf optique et de la choroide, Rec. d'opht. **31**:103, 1909.

36. Juler, F. A.: Hyaline Bodies at the Optic Disc, Tr. Ophth. Soc. U. Kingdom **34**:177, 1914.

37. Lawson, G.: Syphilitic Choroido-Retinitis with Peculiar Growths at the Fundus, Tr. Ophth. Soc. U. Kingdom **3**:117, 1883.

38. Löhlein, W.: Ueber die kegelförmige Papille mit Drusenbildung, Klin. Monatsbl. f. Augenh. **86**:433, 1931.

39. Demaria, B.: Zur Pathogenese der Amotio chorioideae nach Iridektomie bei Glaukom und über Corpora amylacea in der exkavierten Papille, Klin. Monatsbl. f. Augenh. **42**:339, 1904.

40. Athens, A. G.: Glaucoma Associated with Hyaline Bodies (Drusen) of the Optic Disc, Am. J. Ophth. **24**:1138, 1941.

41. Hirschberg, J., and Birnbacher, A.: Beiträge zur Pathologie des Sehorgans, Zentralbl. f. prakt. Augenh. **9**:65, 1885.

42. Wedl, C., and Bock, E.: Pathologische Anatomie des Auges, Vienna, C. Gerold's Sohn, 1886.

43. Rath, W.: Geschwülste der Hypophysis cerebri, Arch. f. Ophth. **34**:81, 1888.

44. Nieden, A.: Drusenbildung des Optikus, Ztschr. f. Augenh. **3**:361, 1900.

45. Fejér, J.: Ueber die Drusen des Sehnervenkopfes, Arch. f. Ophth. **72**:454, 1909.

46. Stood, W.: Zwei Fälle über Drusenbildungen am intraoculären Sehnervenende, Klin. Monatsbl. f. Augenh. **21**:506, 1883.

47. Mendel, F.: Ueber Drusenbildungen im Sehnervenkopf, Zentralbl. f. prakt. Augenh. **24**:242, 1900.

48. Rabitsch, F.: Zur Kenntnis der Drusen im Sehnervenkopf, Klin. Monatsbl. f. Augenh. **43**:72, 1905.

49. Shumway, E. A.: Hyaline Bodies on Optic Nerve Head, Tr. Coll. Physicians Philadelphia **38**:377, 1916.

50. Streiff, J. J.: Ueber Entstehung der Optikusdrusen, Klin. Monatsbl. f. Augenh. **42**:149, 1904.

Fejér,[45] Lordan,[51] Höeg,[11] Juler [36] and Reese.[2] In the case described by Juler central scotoma was also present. Enlargement of the blindspot has been frequently encountered with drusen. This is especially noteworthy, since it shows that enlargement of the blindspot cannot be relied on to differentiate papilledema from the pseudoneuritis produced by drusen of the optic nerve.

It is with particular interest that our attention is drawn to the association of drusen with changes in the fundus in which the optic disk alone is affected. Optic nerve atrophy was described by Müller,[1] Lauber,[5] Remak,[30] Stood,[46] Streiff [50] and Thomson.[52] Optic neuritis was reported by Stood,[46] Sachsalber [26] and Juler.[36] Pseudoneuritis was observed by Bonhoff.[53] Papilledema was recorded by Streiff,[50] Hirschberg and Cirincione [23] and Purtscher.[54] Any of the aforementioned alterations of the optic disk may be sufficiently great that the existence of an intracranial neoplasm must be seriously considered.

The not infrequent occurrence of headaches as a conspicuous symptom in cases of drusen of the optic nerve has previously received scant notice. A survey of the literature discloses that headaches were specifically mentioned as occurring in 6 cases reported by Jany,[55] de Schweinitz,[25] Höeg,[11] Oeller,[14] Stood,[46] and Cibis [34] and in 2 cases reported by Reese.[2] Our 2 cases may be added to this group; they clearly illustrate the clinical importance of appreciating the fact that drusen of the optic nerve may be associated with headaches so severe that the diagnostic possibility of a cerebral tumor must be seriously considered. This is even more true when the appearance of the optic disk is such as to be confused with that of optic neuritis or papilledema. No adequate explanation has been offered for the occurrence of these headaches, and we are unable to elucidate this problem at present.

SUMMARY AND CONCLUSIONS

The clinical records of a man and a woman with drusen of the optic nerves demonstrate the fact that this generally benign neuro-ophthalmologic disorder may at times be characterized by symptoms and signs which closely resemble those usually associated with tumor of the brain. Conspicuous among these clinical manifestations are (1) headache; (2) obscuring of the margins of the optic disk, with at times elevation of the disk, and (3) various alterations of the visual field, usually including enlargement of the blindspot.

Although further clarification is required in order accurately to define the origin of drusen, it is important to recognize the problem at times presented in differential diagnosis.

255 South Seventeenth Street.

4001 West Girard Avenue.

111 North Forty-Ninth Street.

DISCUSSION

Dr. William Zentmayer, Philadelphia: The accumulation of hyalin bodies on the head of the optic nerve is rare, and the scarcity of this condition makes worth while the report of cases. I have 2 such cases that I should like to put on record.

In the first case, a woman aged 23 was referred to me from Florida in May 1942. She had been under an ophthalmologist's care since July 1928. In 1931 there was an appearance of pseudopapillitis, but it was not until 1939 that the present condition was noted in its incipiency. In April 1942, the ophthalmologist gave in detail an accurate description of the condition. The visual fields were contracted and showed a number of reentering angles. Suspecting organic trouble, he had the patient given a thorough physical examination, which revealed a renal disturbance, the exact diagnosis of which was not stated, but the urine had persistently high albumin content, with blood cells.

The patient was normal mentally and presented no physical defects. Vision with correction was 6/4 part in the right eye and 6/6 part in the left eye. The intraocular tension was in the lower range of normal. Examination of the right eye revealed clear media, with a mass of hyalin matter, resembling a white mulberry, on the upper portion of the disk. The mass lay beneath the vessels, and there was some extension on to the retina. In the left eye, the appearance of the disk was similar, but the changes were not so conspicuous as those in the right eye. In both eyes the retinal arteries were too bright.

The visual fields showed considerable irregular contraction with great enlargement of the blindspot, the right field presenting several reentering angles and the left field but one. There could be little doubt that the condition was drusen of the nerve head. Similar anomalies of the fields have been noted before by other investigators, the explanation being that the mass makes pressure on the retinal fibers as they emerge from

51. Lordan, J. P.: Drusen of the Papilla, Am. J. Ophth. **15**:964, 1932.

52. Thomson, E. S.: A Case of Colloid Degeneration of the Optic Nerves, Post Graduate **14**:954, 1898.

53. Bonhoff, J. K.: Bericht uber die Wirksamkeit der Universitäts—Augenklinik zu Giessen, Inaug. Dissert., Giessen, Kindt, 1906.

54. Purtscher, O.: Drusenbildung im Sehnervenkopf, Zentralbl. f. prakt. Augenh. **15**:292, 1891.

55. Jany, L.: Zur Casuistik der Drusenbildung in der Lamina vitrea chorioideae an der Papilla nervi optici, Zentralbl. f. prakt. Augenh. **3**:167, 1879.

the disk. As the history indicated that the condition was recently acquired and was progressive, there is a remote possibility that central vision may later be impaired by pressure on the papillomacular bundle of fibers.

In the second case the condition was more spectacular. A boy aged 9 years was referred by an ophthalmologist from New Jersey. The history was without significance. The child was somewhat undernourished, but there was no history of convulsions; his mentality was good, and there was no adenoma sebaceum. In the right eye the media were clear. Covering all but a narrow rim of the optic papilla, and extending somewhat below the lower border of the papilla on to the retina, was a heap of hyaline globular bodies. The size varied, but the average diameter was about that of a retinal vein, the larger ones being at the lower portion of the mass. The appearance of the whole was that of a white mulberry. The bodies were almost transparent and projected 5 D. into the vitreous. The level of the fundus was emmetropic. At the temporal border of the disk, the crystals were banked in two levels, and between the two the inferior temporal vein emerged. The nasal vein was pushed up somewhat at the edge of the disk. The rest of the fundus was normal. After homatropine had been instilled, the vision in the right eye, without a lens, was 6/6.

The fundus of the left eye presented no anomalies.

I have no recent notes regarding the progress in these cases. Mass drusen of the nerve are uncommon, as shown by the fact that the men who saw these 2 patients had had many years of experience in ophthalmoscopy, but apparently neither of them had ever seen such a condition.

The first patient had pseudo-optic papillitis. As the patient was under observation for several years before the appearance of the hyaline masses on the disk, it is possible that the pseudopapillitis observed in 1931 was due to the presence of these hyaline masses in the optic nerve and that later the increase became apparent on the surface of the papilla.

There should be no difficulty in diagnosing this condition, although in cases of tuberous sclerosis the gross ophthalmoscopic appearance is similar, sometimes even having been described as "mulberry-like"; if only a single lesion involves the nerve head, the resemblance is close. However, the general symptoms of tuberous sclerosis at once clear up the diagnosis.

Dr. Nathan S. Schlezinger, Philadelphia. It is the case in which the drusen are more deeply situated and the appearance of the fundus resembles pseudoneuritis that presents the neurologic problem, especially if headaches of the type present in the second case are prominent. In such cases there may be elevation of the optic disk and enlargement of the blindspot, but drusen are not visible ophthalmoscopically.

UVEITIS ASSOCIATED WITH HODGKIN'S DISEASE

REPORT OF A CASE

SAMUEL KAMELLIN, M.D.
CHICAGO

Uveitis associated with Hodgkin's disease has not, to our knowledge, been reported previously in the literature. Uveitis associated with Boeck's sarcoid (sarcoidosis) has been noted.

Hodgkin's disease [1] is of interest because the etiologic factor is unknown; the condition has been called (1) an atypical form of tuberculosis, (2) an infection, (3) a tumor and (4) a transition between a granuloma and a tumor.

Clinically the disease may appear between the ages of 6 months and 76 years. It is most common, however, between the third and the fourth decade of life and occurs twice as frequently in men as in women. The average duration of the disease is eighteen months, but in the chronic form it may last for years.

It is usually thought of as a condition affecting the lymph glands of the neck, but involvement of the abdominal and thoracic nodes is more frequent. The spleen is involved in 60 to 75 per cent of cases. The blood picture shows a progressive anemia, with no change in the leukocytes and sometimes an increase in the eosinophils.

The differential diagnosis is made by examination of an involved lymph node, and the diseases to be considered are glandular tuberculosis, lymphosarcoma and Boeck's sarcoid.

Microscopically the essential change is a proliferation of the reticuloendothelial cells, which gradually replace the lymphocytes. The new cells are large and pale, with vesicular nuclei of the epithelioid type. More characteristic are the large giant cells, many of which are mononuclear and many multinucleated. These giant cells are known as Dorothy Reed cells, or Sternberg cells. The feature which distinguishes Hodgkin's disease from lymphosarcoma is the involvement in the latter of one group of nodes, with the subsequent spread of the condition by direct continuity to another group of lymphoid structures.

Microscopically lymphosarcoma shows complete replacement of mature lymphocytes by much larger, hyperchromatic cells with a small amount of basophilic cytoplasm and a round or oval nucleus with a fairly prominent nucleolus. Uniformity of cell type is an outstanding feature, in contrast to the multiplicity of cell forms present in Hodgkin's disease. In addition to lesions of the lymph nodes, the lymphoid tissue in the pharynx, gastrointestinal tract, spleen, bone marrow, liver and other organs is widely involved. The blood picture is that of a progressive secondary anemia, but there may be relative or absolute lymphocytosis.

In tuberculosis the typical cell is the epithelioid cell, which forms the principal part of the tubercle.

The clinical picture in Boeck's sarcoid simulates that of Hodgkin's disease. This condition is known to involve the uveal tract of the eye and the skin, lymph nodes, myocardium, pancreas, tonsil, parotid and lacrimal glands. The lesions are circumscribed masses resembling miliary tubercles, the chief components of which are epithelioid cells, with macrophages, giant cells and occasional eosinophils. The giant cells are larger than those of tuberculosis and contain more nuclei.

The roentgenographic features of Hodgkin's disease and of lymphosarcoma are enlargement of the hilar glands, with no involvement of the substance of the lungs; those of tuberculosis are infiltration and cavity formation, involving usually the apexes and bases of both lungs. In sarcoidosis the infiltration is along the bronchial tree and simulates most closely the picture of miliary tuberculosis.

REPORT OF CASE

Mr. C. D., aged 26, was admitted to the service of Dr. Sanford R. Gifford at Wesley Memorial Hospital on March 25, 1943. His complaint was that of failing vision for the past three months. At first he could not make out faces of people he knew and later was unable to read the newspaper. Three to four weeks prior to his admission to the hospital for this trouble he went to his family physician because of a swelling in his neck. His physician advised that he go to the

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The late Dr. Sanford R. Gifford advised me in the report of this case.

From the Department of Ophthalmology, Northwestern University Medical School.

1. Boyd, W.: The Pathology of Internal Diseases, ed. 3, Philadelphia, Lea & Febiger, 1940.

hospital for surgical removal of a gland from the mass for pathologic study. Biopsy revealed considerable fibrosis and some hyalinization of fibrous tissue. Dorothy Reed cells and a few eosinophils were scattered throughout the section. The pathologist's diagnosis was chronic Hodgkin's disease (fig. 1).

lamp revealed cells in the anterior chamber and pigment and cell deposits on the anterior capsule of the lens. The patient was given a solution of scopolamine to use; after he stopped taking the drug, his pupils decreased in size and became adherent to the anterior capsule of the lens. The pupils were then dilated with

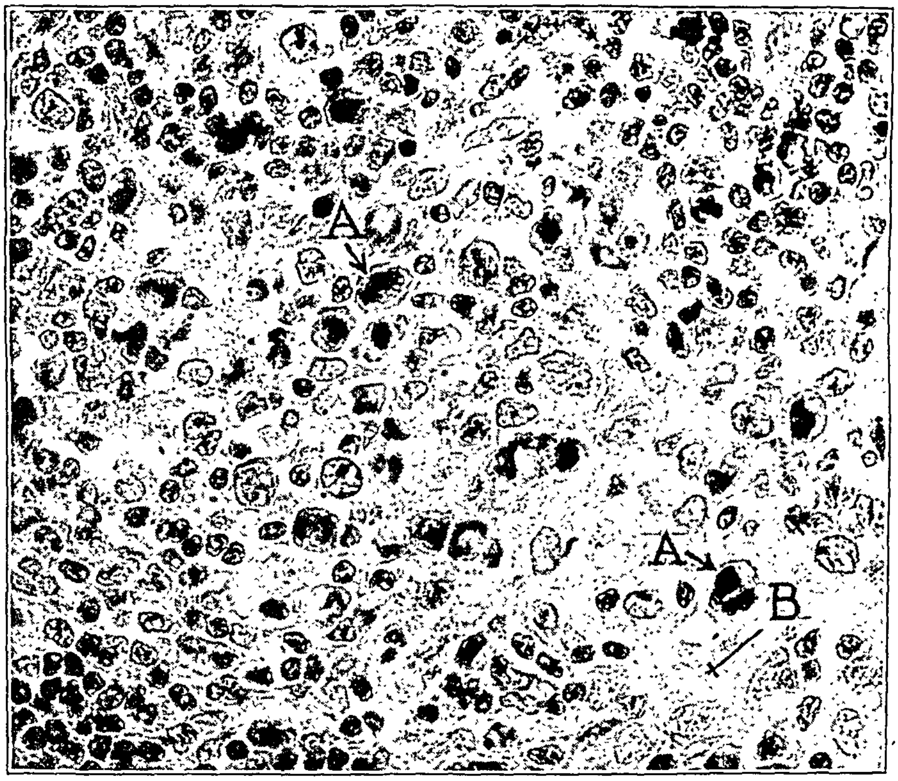

Fig. 1.—Section of a cervical lymph node, showing (*a*) Dorothy Reed cells and (*b*) fibrosis.

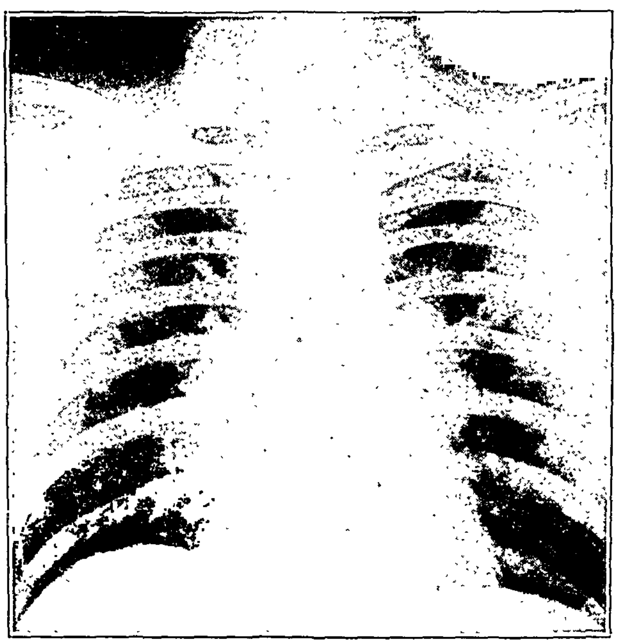

Fig. 2.—Roentgenogram of the patient's chest, showing involvement of the hilar lymph nodes. The apexes and the peribronchial regions are infiltrated.

Roentgenograms of the chest revealed the changes typical of Hodgkin's disease of the hilar lymph nodes (fig. 2).

Previous to his admission to the hospital, he was seen by Dr. Gifford in his office. Examination with the slit

neosynephrine and were kept free by administration of small doses of scopolamine. During this interval there was mild superficial and deep congestion of the vessels.

On his admission to the hospital, visual acuity was limited to ability to count fingers at 1 foot (30 cm.)

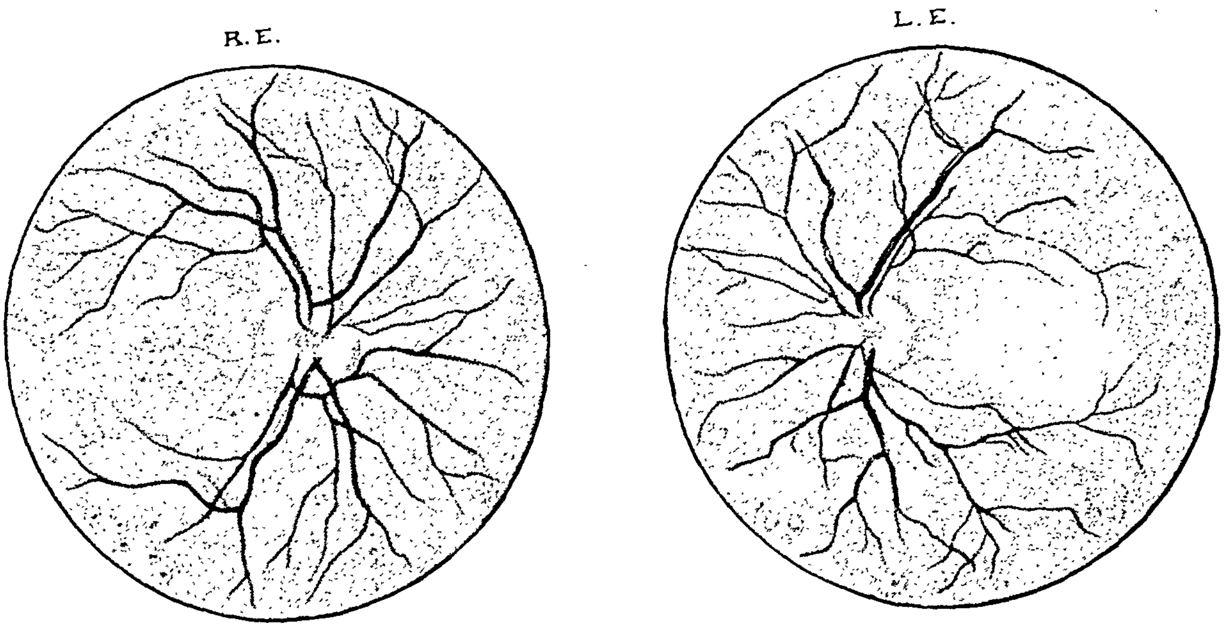

Fig. 3.—Drawing, showing large gray areas in the macular regions, with white deposits in the periphery of each fundus.

with the right eye and was 1/50 in the left eye. External examination revealed nothing abnormal. Examination of the fundi and media by Dr. Gifford revealed a great number of opacities in the vitreous of both eyes. Large gray areas were present in both macular regions; no vessels were visible. There were also many small white deposits in the periphery of each fundus. Above the left fovea was a small white area which elevated the vessels near it (fig. 3).

General physical examination showed essentially nothing unusual except for the presence of a small scar on the neck where the gland had been removed. The mass previously observed in the neck was gone, its disappearance being attributed to the roentgen ray therapy which he had received.

The red blood cells numbered 5,340,000 and the white blood cells 13,350 per cubic millimeter, and the hemoglobin concentration was within normal range. Urinalysis gave normal results.

The Frei, brucellin and tuberculin cutaneous tests gave negative reactions.

The patient was placed under treatment with nonspecific foreign protein, typhoid and vaccine paratyphoid A and B being given. On his discharge from the hospital visual acuity was 8/50 in the right eye and 1/50 in the left eye, values showing improvement in the right eye and no appreciable improvement in the left eye.

The patient has since been followed closely, and on his last examination, on Dec. 16, 1943, visual acuity was 6/200 in the right eye and 3/200 in the left eye. At the time of writing the vitreous still shows many opacities. There are still large grayish areas in the macular regions from which finger-like processes extend into the vitreous. A number of flat, white areas in the periphery and macular regions resemble those seen in cases of miliary tuberculosis.

General examination of the palpable lymph glands has revealed no further enlargement to date, and the patient's condition is good.

Whether the uveitis accompanying Hodgkin's disease in this case is due to the latter condition or is a concomitant disease is not clear. Since, however, the tests and examinations did not reveal any positive indication of other disease and there is pathologic and roentgenographic evidence of Hodgkin's disease, we are inclined to believe that the ocular condition is due to Hodgkin's disease.

UVEITIS; DYSACOUSIA; ALOPECIA; POLIOSIS, AND VITILIGO

A THEORY AS TO CAUSE

ELIOTT B. HAGUE, M.D.
BUFFALO

Because the most disabling manifestation of the rare disease complex under consideration is ocular, it is not surprising that the syndrome has been discussed chiefly in the ophthalmologic literature. Still, the existence of the syndrome, and certain aspects of it which have not always been widely recognized, demonstrate the relevance of systemic and ocular disease. The repeated occurrence of the disease pattern should interest the nosologist, who still must hesitate to designate it as a disease entity, when most or all of the same clinical picture may follow severe emotional trauma, expansion of an ependymoma of the third ventricle and, frequently, transient encephalitis. Certainly, the subject is of interest to the internist, the dermatologist and the neurologist.

In this paper the historical background of the syndrome is briefly reviewed. A general description of the disease picture is presented, including the fact that the prodrome may be essentially either an encephalitis or a severe emotional disturbance, the latter suggesting the possibility of hypothalamic involvement, which if present is of far reaching interest. A remarkably similar clinical picture has been produced by impingement of a tumor of the third ventricle on the hypothalamus. A case of the syndrome is presented, with photographs taken with ultraviolet light showing the vitiligo. Certain manifestations involving the skin are shown to be associated with other disease states, to be, in all probability, true dermatoneuroses, and to be comparable to depigmentation affecting the eye in this syndrome. The "depigmentation" of ocular tissue constitutes a disturbance of pigment deposit more severe and more generalized than is common with sarcoma of the choroid; and since the latter lesion has, even before 1878, been known to cause sympathetic ophthalmia,[1] it is suggested that the inflammatory disease picture in the eye in this syndrome, remarkably similar to that observed in sympathetic ophthalmia, is secondary to pigment changes. Lastly, the basis for the belief that the hypothalamus may be the primary seat of the syndrome is presented, and evidence that a virus may cause the hypothalamic involvement is referred to. The results of cisternal inoculation of rabbits with material taken from the patient's eye over a year after the acute stage of the disease are mentioned.

HISTORICAL REVIEW

Depigmentation of the cilia and eyebrows, frequently sudden, and following supraorbital neuralgia, painful trauma or nontraumatic severe intraocular inflammation, has long intrigued ophthalmologists. The earliest reference to whitening of the cilia which I have found is that of Ali ibn Isa, whose text Wood[2] imputed to the period 940-1010 A. D. Considerably later (in the twelfth century) another Arab physician,[3] referred to by Babel[4] and others, in dealing with the historical aspect of the syndrome, mentioned canities in a list of thirty-seven apparently common ocular disorders. Schenkl[5] was the first to report its appearance during the course of "sympathetic ophthalmia." Other early papers on the subject have been reviewed by Babel,[4] who did not refer specifically to Jonathan Hutchinson's[6] account, in 1892, of "blanched eyelashes"

Read at the meeting of the Medical Society of the State of New York, Section on Ophthalmology and Otolaryngology, Buffalo, May 5, 1943.

1. (*a*) Duke-Elder, W. S.: Text Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, p. 2329-2332. (*b*) Mauthner, L.: The Sympathetic Diseases of the Eye, translated by W. Webster and J. A. Spalding, New York, W. Wood & Co., 1881, p. 44.

2. Wood, C. A.: Memorandum Book of a Tenth-Century Oculist for the Use of Modern Ophthalmologists: A Translation of the Tadhkirat of Ali Ibn Isa of Baghdad (cir. 940-1010 A. D.), the Most Complete, Practical and Original of All the Early Textbooks on the Eye and Its Diseases, Chicago, Northwestern University, 1936, p. 102.

3. Mohammad, Al-Ghâfiqi: Le guide d'oculistique: 1100-1200 A. D., translated by M. Meyerhof, Barcelona, Laboratories du Nord de l'Espagne Directeur, Masnou, 1933, pp. 22 and 46.

4. Babel, J.: Syndrome de Vogt-Koyanagy (uvéite bilaterale, poliosis, alopecie, vitiligo et dysacousie), Schweiz. med. Wchnschr. **69**:1136, 1939.

5. Schenkl, A.: Ein Fall von plötzlich aufgetretener Poliosis circumscripta der Wimpern, Arch. f. Dermat. u. Syph. **5**:136, 1873.

6. Hutchinson, J.: A Case of Blanched Eyelashes, Arch. Surg., London **4**:357, 1892-1893.

in cases of severe bilateral uveitis, the earliest mention of the subject in English.

From that time, various authors have made similar observations, sometimes associating the uveitis, which is more or less severe,[7] and the depigmentation of the cilia and superciliary region with difficulties of hearing and with alopecia areata, which is followed by regrowth of hair, now white, in the involved areas. Koyanagi,[8] in 1929, summed up the observations of 14 Japanese authors in tabular form, and subsequently histologic and bacteriologic studies have appeared in their literature. Parker [9] in 1931, published the first description in the English language except for Hutchinson's brief note; he summarized 19 cases, including 2 of his own, and cogently commented that "the [reported] incidence of neuroretinitis and detached retina may be far from correct, as a satisfactory fundus examination is impossible in many cases." He commented on the similarity of the syndrome to sympathetic ophthalmia, in which a similar uveal involvement may appear and in conjunction with which alopecia, poliosis and deafness have been reported. He extended his comments in a review,[10] published in 1940.

Rones,[11] in 1932, published 3 typical cases. He stated that a scratchy feeling often precedes the uveitis in this disease. His observation is confirmed in the case reported here, in which to the patient it seemed a prominent feature of the prodrome.

Davies, [12] in the presentation of a case, succinctly reviewed the etiologic theories which have been proposed. As he stated, the result has usually been negative when tuberculin and Wassermann tests have been performed. The theory submitted by Peters [13] and by Cramer,[14] that anaphylactic toxins formed by the destruction of uveal pigment cause the manifestations in the skin, hair and ear, has little to recommend it beyond the fact that pigmentary changes do occur in the skin and hair and that similar changes might occur in certain pigmented structures in the cochlea. It does not account for the prodromal encephalitis, or explain why, if the eye were the seat of the primary lesion, apparently similar intraocular disease in other forms of uveitis does not involve the hair, skin and ears. While Cramer reported that intravenous injections of blood from affected subjects into rabbits produced poliosis in these animals, any such changes might be explained on an *infective basis.*

In 1939 Babel [4] collected 46 cases of the syndrome. A number of these cases, particularly the earlier ones, do not seem entirely typical, but it may be that some of them were not completely reported. It is certain that the constellation of bilateral uveitis, dysacousia, alopecia areata, poliosis and vitiligo appears too constantly to be regarded as simple coincidence.

Since that time cases have been reported by Zentmayer [15] and by Carrasquillo.[16]

GENERAL DESCRIPTION

The ensemble of symptoms is too consistent to suggest a heterogeneous pathogenesis. Just as in other clearly defined disease states certain manifestations may atypically be added to, or be absent from, the clinical picture in individual cases, so with this syndrome abbreviated versions have been reported, some of these variants shading into significantly related disease. The syndrome bears striking resemblance in certain respects to Harada's disease (bilateral detachment of the retina associated with low grade uveitis) and to sympathetic ophthalmia.

In the earlier case reports medical observers appear to have been more frequently aware of the severe uveitis and the striking poliosis than of the alopecia, vitiligo or dysacousia. Other manifestations equally typical of the syndrome, and probably equally significant, have received still less attention.

It is likely that many cases of the apparently incomplete syndrome were actually cases of the fully developed disease, meagerly reported. Some of the symptoms associated with this syndrome do not present themselves dramatically to either patient or physician and may have been overlooked in some instances. Other relevant aspects are mentioned in careful case reports without

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7. Compare the related syndrome Harada's disease.
8. Koyanagi, Y.: Dysakusis, Alopecia und poliosis bei schwerer Uveitis nicht traumatischen Ursprungs, Klin. Monatsbl. f. Augenh. **82**:194, 1929.
9. Parker, W. R.: Uveitis Associated with Alopecia, Poliosis, Vitiligo and Deafness, Am. J. Ophth. **14**:577, 1931.
10. Parker, W. R.: Severe Uveitis with Associated Alopecia, Poliosis, Vitiligo and Deafness, Arch. Ophth. **24**:439 (Sept.) 1940.
11. Rones, B.: Uveitis with Dysacousia, Alopecia and Poliosis, Arch. Ophth. **7**:847 (June) 1932.
12. Davies, W. S.: Uveitis with Associated Alopecia, Poliosis, Vitiligo and Deafness, Arch. Ophth. **14**:239 (Aug.) 1935.
13. Peters, A.: Die Diagnose und Therapie der sympathischen Augenentzündung, Deutsche med. Wchnschr. **38**:*1361, 1912*; cited by Davies.[12]
14. Cramer, E.: Zur Frage der anaphylaktischen Entstehung der sympathischen Entzündung, Klin. Monatsbl. f. Augenh. **51**:*205, 1913.*
15. Zentmayer, W.: Severe Uveitis with Associated Alopecia, Poliosis, Vitiligo and Deafness, Arch. Ophth. **27**:342 (Feb.) 1942.
16. Carrasquillo, H. F.: Uveitis with Poliosis, Vitiligo, Alopecia and Dysacousia (Vogt-Koyanagi Syndrome), Arch. Ophth. **28**:385 (Sept.) 1942.

being given significant emphasis or being considered related to the illness. None the less, there is a good deal of variation in the severity and inclusiveness of the syndrome, and cases have been reported in which one or more of the classic features have on careful search proved to be absent.[17]

It is even probable that abortive cases do occur. In addition to the case here reported (of the complete syndrome), it has been my privilege, through permission of Dr. John Dunnington, to study a case in which only much less severe uveitis, retinal detachment and poliosis of the cilia and brow were present. When the plastic iritis is more striking, the similarity to sympathetic ophthalmia is greater, and it is historically interesting that numerous observers have noted the clinical resemblance.[12]

In typical cases the first symptoms to appear are ocular, sometimes a scratchy feeling being first noticed in the eyes, as Rones [11] reported and as was noted in the case to be described here, followed by lowering of visual acuity. In a number of cases in which the fundus has been observed in an early stage of the disease, papillitis and retinal edema, choroidal disturbance and day blindness have been observed. Opacities, generally fine, appear in the vitreous; and anterior uveitis develops, with keratitic precipitates, seclusion and occlusion of the pupil. The plastic exudate in the anterior chamber may be pronounced. The iridocyclitic reaction persists in its inflammatory phase for months, terminating in pronounced atrophy of the pigmented structures, as shown by transillumination or ophthalmoscopic examination. Because of the intense intraocular damage, in the more severe forms of the disease visual acuity does not improve, and even if phthisis bulbi does not appear, as it often does, virtual or complete blindness is the end result in most cases. It is my impression that the degree of severity of the intraocular process tends rather uniformly to be equal in the two eyes of the individual patient. Secondary glaucoma or retinal detachment may be encountered.

In both typical and, as it were, abortive cases there is, time and again, a prodrome of an influenza-like episode.[18] But in a case reported by Laje Weskamp,[19] in which the influenzal prodrome was not present, transcendent emotional trauma immediately preceded the onset of the disease. The fact that all, or practically all, the manifestations of this syndrome have followed (*a*) an infection of the upper respiratory tract suggesting encephalitis, (*b*) severe emotional trauma or (*c*) a tumor pressing on the hypothalamus deserves later comment.

As early as 1890, Bock [18a] reported a case of optic nerve atrophy occurring ten days after an attack of "influenza" and suggested that transient localized meningitis in the region of the chiasm was responsible for the nerve lesion. In this case, as in others,[20] poliosis of the cilia developed after an initial attack of influenza.

The "influenza" in the more completely reported cases appears to have been encephalitis.[21] Since persistent headaches,[21a] drowsiness, unmitigated by ordinary medication, gastrointestinal upset with vomiting, fever,[22] and even delirious shivering,[23] were present, a positive Queckenstedt sign would appear characteristic of this stage (it may be assmed that a block in the circulation of the cerebrospinal fluid accounts for the cephalgia). The presence of hypercholesteremia and hyperglycemia has been reported.[24] At this stage, in 1 case, a roentgenogram gave evidence of increased intracranial pressure.[23a]

17. (*a*) Jess, A.: Poliosis, Vitiligo, und doppelseitige schwerste Iridocyclitis bei Dystrophia adiposo-genitalis, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **49**: 469, 1932. (*b*) Koyanagi.[8]

18. (*a*) Bock, E.: Ueber frühzeitiges Ergrauen der Wimpern, Klin. Monatsbl. f. Augenh. **28**:484, 1890. (*b*) von Michel, J.: Die Krankheiten der Augenlider, in Graefe, A., and Saemisch, E. T.: Handbuch der Augenheilkunde, ed. 2, Leipzig, Wilhelm Engelmann, 1908, vol. 5, pt. 2, p. 294. (*c*) Jess.[17a]

19. Laje Weskamp, R.: Uveitis exudativa bilateral con disacusia, poliosis, alopecia y desprendimiento retiniano, Rev. Asoc. méd. argent. **46**:1451, 1932.

20. Jess.[17a] von Michel.[18b]

21. (*a*) Krasnoff, M. L.: Uveitis, Vitiligo, Poliosis, Dysacousia, in Sbornik v oznamenovanie sorokaletiya nauchnoy deyatelnosti zasluzhennogo deyateya nauki M. I. Averbakha, Moscow, Gosudarstvennoe izdatelstvo biologischeskoy i meditsinskoy literatury, 1935, p. 244; abstracted, Zentralbl. f. d. ges. Ophth. **37**:120, 1937. (*b*) Bunge, E.: Ueber doppelseitige Iridozyklitis und Poliosis, Arch. f. Augenh. **108**:212, 1933. (*c*) Calogero, G.: Sui disturbi auricolari nell'oftalmia simpatica, Arch. di ottal. **33**:499, 1926. (*d*) Avalos, E.: Un neuvo caso de uveitis bilateral grave acompañado de sordera, calvicie y canicie, Rev. cubana de oto-neuro-oftal. **1**:242, 1932; Mi tercera observación sobre un caso de uveitis bilateral grave, acompañado de sordera, calvicie y canicie, ibid. **5**:75, 1936. (*e*) Magitot, A., and Dubois-Poulsen, A.: Un cas de syndrome de Harada uvéite grave avec décollements bilatéraux et encéphalite, Bull. Soc. d'opht. de Paris **51**:223, 1939. (*f*) Soriano, F. J.: Sordera, calvicie y canicie an las uveitis bilaterales graves, simpáticaso no, Arch. de oftal. de Buenos Aires **4**:537, 1929. (*g*) Vonderahe, A. R.: Changes in the Hypothalamus in Organic Disease, A. Research Nerv. & Ment. Dis., Proc. **20**:689, 1940. (*h*) Babel.[4] (*i*) Bock.[18a]

22. Calogero.[21c] Magitot and Dubois-Poulsen.[21e]

23. (*a*) Yanes, T. R., and Ferrer, O.: Uveitis doble espontanea, con disacusia, alopecia y poliosis, Rev. cubana de oto-neuro-oftal. **7**:5, 1938. (*b*) von Michel.[18b]

24. Aten, A. H.: Ueber Poliosis und Iridozyklitis, Ophthalmologica **97**:265, 1939.

In the few cases in which a spinal tap was performed shortly after the onset of the complaint which first brought the patient under medical observation, a rather pronounced pleocytosis was noted, but the spinal fluid has been examined early in too few instances of this rare disease for the establishment of more than the probability that pleocytosis will be found if searched for not long after the onset of the prodrome.[25] The case to be reported shows how transient this abnormality of the spinal fluid may be.

In some cases severe emotional trauma antedated the prodrome.[26] Its etiologic significance must be suspected in the sporadic cases in which circumstances, such as sudden dread of imminent death, either of the patient or of some member of the family, have been followed by rapid whitening of the hair, as in the imperfectly authenticated case of Marie Antoinette, or, within a few days, by the uveitis, complicated shortly by all the rest of the syndrome, including optic neuritis, retinal detachment, dysacousia, poliosis, alopecia and vitiligo. Parker[27] stated that it is not possible to determine how frequently retinal detachment and neuroretinitis occur in such cases, for frequently a satisfactory examination of the fundus cannot be made when the patient is first observed. In 1 case,[19] a laborer in the Argentine, falling into a deep pit, caught himself on a timber after falling a few feet and clung there for a good portion of an hour, without much expectation of rescue. When he was extricated, he was observed to remain in great terror, was "covered with cold sweat" and complained immediately of severe headache and tinnitus on the right side. In this case, in which the etiologic mechanism seems to have been functional rather than "influenzal," not only did the alopecia and dysacousia disappear, as they do in most cases, but the ocular manifestations, which ordinarily do not show recovery, here exhibited pronounced improvement. The retina became completely reattached, and vision improved from perception of light in either eye to visual acuity of 1/8 in the right eye and 1/6 in the left eye. Although recovery of this degree of vision may not appear striking, most patients with this symptom complex do not maintain more than ability to perceive hand movements.

When the signs of an encephalitic process are pronounced, there may be disturbance of the sleep rhythm, a complaint traceable to a lesion in the basal ganglions, which are held to mediate the various phenomena of sleep. The severity of the encephalitis at this stage appears to vary; often when the patient is first seen the presenting complaint is blurring of vision. If the patient is examined while the ocular media are still clear, a low degree of papillitis or depigmentation of the chorioretina may be observed.

Contraction of the visual fields[28] and night blindness[29] have been reported more frequently than have normal fields of vision or normal light sense. When it has been possible to observe the retina, pathologic processes (papillitis, retinal exudation and degeneration) sufficient to account for severe functional impairment have been seen.[30] Although it may appear difficult to classify the various retinal changes reported under one pathogenic heading, conspicuous depigmentation of the fundus has been repeatedly observed.[31] Franceschetti and Valerio[32] reported the association of heterochromia iridis with the dysraphic status and vitiligo. Other investigators mentioned the associated occurrence of heterochromia iridis.[33] When transscleral transillumination was employed, pronounced rarefaction of pigment was seen in all parts of the uvea except the ciliary zone.[19] This change was present in the case here reported. Soon the ocular picture is that of an anterior and a posterior uveitis. Seclusion or occlusion of the pupil, in greater or less degree, usually follows, and it is because many of the patients in the recorded cases were first seen at this stage that much uncertainty exists regarding the earlier neuroretinitis. Keratitic precipitates, floating bodies in the vitreous and seclusion and occlusion of the pupil, in greater or less degree,

25. (*a*) Malbrán, J., and Muhlmann, V.: Enfermedad de Harada, Cong. argent. de oftal. (1936) **2**:194, 1938. (*b*) Avalos.[21d] (*c*) Bunge.[21b] (*d*) von Michel.[18b] (*e*) Steindorff, K.: Vitiligo der Lider und Poliosis nach stumpfer Verletzung, Klin. Monatsbl. f. Augenh. **53**: 188, 1914.

26. Avalos.[21d] Yanes and Ferrer.[23a]

27. Parker, footnotes 9 and 10.

28. (*a*) Erdmann, P.: Zur Frage eines Zusammanhanges zwischen Vitiligo und Augenliden, Klin. Monatsbl. f. Augenh. **49**:129, 1911. (*b*) Laje Weskamp.[19] (*c*) Magitot and Dubois-Poulsen.[21e]

29. Laje Weskamp.[19] Avalos.[21d]

30. (*a*) Gilbert, W.: Vitiligo und Auge, ein Beitrag zur Kenntnis der herpetischen Augenerkrankungen, Klin. Monatsbl. f. Augenh. **48**:24, 1910; Ueber Bezeihungen der Gefasshaut zu endokrinen Störungen, Ber. u. d. Versamml. d. deutsch. ophth. Gesellsch. **48**:26, 1930. (*b*) Laje Weskamp.[19] (*c*) Magitot and Dubois-Poulsen.[21d] (*d*) Soriano.[21f]

31. (*a*) Komoto, J.: Ueber Vitiligo und Auge, Klin. Monatsbl. f. Augenh. **49**:139, 1911. (*b*) Wexler, D.: Ocular Depigmentation Accompanying Generalized Vitiligo, Arch. Ophth. **57**:393, 1928. (*c*) Babel.[4] (*d*) Laje Weskamp.[19] (*e*) Magitot and Dubois-Poulsen.,[21e] (*f*) Erdman.[28a]

32. Franceschetti, A., and Valerio, M.: L'uveite recidivante (ad ipopion) manifestazione parziale di una sindrome muco-cutaneo-oculare, Rassegna ital. d'ottal. **9**:1, 1940.

33. Erdmann.[28a] Babel.[4]

usually follow.[34] In some, but not in all, cases there is retinal detachment.[35]

Late in the course of the disease examination with the corneal microscope and the slit lamp has shown marked atrophy of the iris, with dispersion of pigment.[21c] This lesion was also conspicuous in my case. Whether the heavy posterior synechia indicates an inflammatory, as well as a degenerative, process merits study and consideration.

By this time the dysacousia, which may occur as early as during the prodromal stage of encephalitis, is usually a source of discomfort to the patient. It consists of usually partial, and often unilateral, deafness, which may persist for several months but which tends to disappear, and of a troublesome ringing in the ears, often unilateral, which lasts longer.

The results of laboratory studies, except those of the spinal fluid, are negative consistently enough to minimize any importance attached to an occasional positive Wassermann reaction [12] or a positive diagnostic tuberculin reaction.

One to three months after the onset of the disease alopecia similar to, or identical with, alopecia areata appears, followed usually, and with the same frequency as is alopecia areata, by poliosis. Although whitening of the hair in a piebald manner is not uncommonly associated with alopecia areata, in cases of this syndrome many of the hairs of the brow and many of the cilia are involved, and occasionally [19] other regions of the body hair are included in this process. The vitiligo usually appears about the time of, or a little after, the alopecia. The fact that the vitiligo is not always conspicuous under ordinary illumination may account for its later recognition, historically, in cases of this syndrome. In a number of early cases the patient came under medical observation rather late in the disease, and this may account for the fact that in these cases alopecia was not mentioned.

As the regrowth of hair occurs in the affected areas, it tends to be white. This, and the generalized vitiligo described by Gilbert,[30a] which is likely to occur broadly in the region of the depigmented brow, as well as on the trunk,[36] or even on the extremities, give the patient a striking and bizarre appearance, which, together with blindness, is apt to cause him much concern. The progress is gradual, extending over many months. In 1 case, a daughter of the patient showed premature graying of the hair, and there was a family history of poliosis.

As previously stated, the changes in the eyes are progressive, and it is months before the uveitis, which varies in severity and is sometimes complicated by secondary abnormalities of intraocular tension, begins to subside.

During the active course of the disease, and later, severe disturbances of temperature sensation have been reported.[37] Previously the cryesthesia had been interpreted as hysterical. In 1 of Gilbert's cases, that of a man aged 35, libido and potency were entirely lost, suggesting hypothalamicohypophysial involvement. Perhaps only apparently relevant to this discussion is Jess's [17a] case, an instance of typical dystrophia adiposogenitalis.

RELATION OF MANIFESTATION

Alopecia.—Alopecia may be due to local disease of the skin [38] or may be secondary to severe systemic illness, or in the form in which it is seen in this syndrome (typical alopecia areata) it was included by Becker and Obermayer [39] among the dermatoneuroses. Parker,[27] similarly, listed the causes of alopecia as infection, reflex neurosis or endocrine disturbance. McCarthy [38] stated that alopecia, of nervous origin, may be the essential primary lesion or may be secondary to atrophic changes in the skin. It is noteworthy that loss of hair following severe systemic illness is frequently a delayed manifestation. It is likely, as Stokes [40] emphatically stated, that "the interplay between emotion and infection, emotion and allergy, emotion and sweat, and vasomotor mechanisms, furnish some of the most complicated of the present problems of increasing importance. . . ." Niles [41] and Becker and Obermayer included alopecia [39] among the dermatoses of neurogenic origin.

McCarthy [38] stated that the actual cause of alopecia is not known. According to him, Bärnsprung suggested as early as 1858 that alopecia may be due to nutritional disturbances of the hair papilla resulting from derangement of trophic nerves serving it. He referred to the work of Joseph and others, who produced alopecia in

34. Magitot and Dubois-Poulsen.[21e] Gilbert.[30a] Komoto.[31a]

35. Magitot and Dubois-Poulsen.[21e] Soriano.[21f] Koyanagi.[8]

36. Luo, T. H.: Uveitis Associated with Alopecia, Poliosis, Dysacousia, and Vitiligo, Chinese M. J. **50:** 1409, 1936.

37. Yanes and Ferrer.[23a] Avalos.[21d] Magitot and Dubois-Poulsen.[21e]

38. McCarthy, L.: Diagnosis and Treatment of Diseases of the Hair, St. Louis, C. V. Mosby Company, 1940, pp. 63 and 137.

39. Becker, S. W., and Obermayer, M. D.: Modern Dermatology and Syphilology, Philadelphia, J. B. Lippincott Company, 1940, p. 533.

40. Stokes, J. H.: Personality Factor in Psychoneurogenous Reactions of the Skin, Arch. Dermat. & Syph. **42:**780 (Nov.) 1940.

41. Niles, N. D., in discussion on Stokes.[40]

experimental animals by section and removal of the sympathetic trunks. Stokes and his associates [42] summarized current criticism of Joseph's technic but concluded that there is a gradually increasing accumulation of evidence that a neural mechanism plays a causative role in loss of hair. That the familiar association of functions of the endocrine and the vegetative nervous system is involved in the production of alopecia, as well as poliosis and vitiligo, is confirmed by the opinion expressed by Genner,[43] McCarthy,[38] Stokes and associates,[42] Becker and Obermayer [39] and others. Von Weo, cited by von Michel,[18b] reported the association of alopecia of the lids with exophthalmic goiter, and Genner pointed out that alopecia frequently occurs with exophthalmic goiter, in certain nervous diseases, disturbances of the vegetative nervous system and after trauma and shock. Galewsky [44] stated that children of parents with exophthalmic goiter often show alopecia or vitiligo or both. There is a considerable literature relating to the endocrine background of alopecia, poliosis and vitiligo.[45] Wyss [46] recorded both alopecia and vitiligo in the affected areas in cases of herpes zoster. Terrien [47] mentioned the association of alopecia and cataract. Alopecia areata has been reported to be associated with syringomyelia and progressive facial hemiatrophy.[48] In a case of alopecia reported by Vonderahe [21g] the hypothalamus showed significant changes. Von Michel [18b] stated that alopecia neurotica may be accompanied by poliosis and may follow local trauma. Donath [49] observed local erythema of the skin and falling of the hair after excision of a segment of a sympathetic nerve. Becker,[50] in a personal communication, suggested that in the case which I am reporting the alopecia is probably neurogenic.

Poliosis.—Poliosis, or canities, is a premature bleaching or whitening of the hair; it may affect all the lashes of one or both eyes or be confined to a small number of cilia. Frequently the eyebrows show a similar depigmentation. The hair of the head and of the body generally may be involved. A good deal has been written about the biochemical change in the hair tissue, and the most complete monograph on this subject is that of Schreiber.[51]

McCarthy [38] maintained that sudden graying of the hair was produced by rapid penetration of the hair by air, a vacuolation ascribed to neural influence; Steindorff [25e] confirmed this in his case, but Vogt [52] could not. Certain forms of poliosis, at least, are considered to be due to inhibition of pigment formation in the cortical cells of the hair-bearing skin.

McCarthy [38] distinguished between "true poliosis," which is permanent, and canities due to alopecia areata, which (frequently) is not permanent. This distinction serves to emphasize the fact that poliosis is frequently, but not always, an accompaniment of, or secondary to, alopecia areata. The causal relation of poliosis and vitiligo has been suggested here.

A survey of many reported cases of graying hair shows that frequently no mention is made of the rapidity of the process or of the duration of the change in color. Poliosis has been observed to occur in persons of all age groups; it has been reported in children 5 years of age.[53] To distinguish between "true poliosis" and secondary poliosis on the basis of permanence is somewhat empiric. Although Oesterlen,[54] as recently as 1931, stated that graying or whitening of the hair occurring overnight or in the course of several days has never been established, and is, in his opinion, impossible, there appears to be sufficient reason to believe that a sudden whitening of the hair does occur. Although some of the earlier instances, such as the case of Marie Antoinette, have been reported by witnesses whose reliability cannot be determined

42. Stokes, J. H.; Beerman, H., and Ingraham, N. R., Jr.: Psychoneurogenous Component of Cutaneous Reaction Mechanisms, Am. J. M. Sc. **198**:577, 1939; **200**:560, 1940.

43. Genner, V.: Études clinique sur la pelade, Copenhagen, Levin & Munksgaard, 1929; cited by Stokes.[40]

44. Galewsky, E.: Beiträge zur Kenntnis Alopecia areata, Dermat. Wchnschr. **81**:1327, 1925.

45. Bauckus, H. H.; Siekmann, C. F., and Kwak, A. V.: Treatment of Alopecia Areata with Thyroid Extract, New York State J. Med. **36**:1629, 1936.

46. Wyss, O.: Beitrag zur Kenntnis des Herpes Zoster, Arch. d. Heilk., 1871, p. 261.

47. Terrien, F.: Troubles visuels et altérations des glandes á sécrétion interne, Arch. d'opht. **39**:716, 1922.

48. Satke, O.: Ueber das Ergrauen der menschlichen Korperbehaarung, Ztschr. f. Konstitutionslehre **15**:646, 1930.

49. Donath, J.: Der Werth der Resection des Halssympathicus bei genuiner Epilepsie, nebst einigen Beobachtungen und physiologischen Versuchen über Sympathicuslähmung, Wien. klin. Wchnschr. **11**:383, 1898.

50. Becker, S. W.: Personal communication to the author.

51. Schreiber, L.: Die Krankheiten der Augenlider, ed. 3, Berlin, Julius Springer, 1924.

52. Vogt, A.: Frühzeitiges Ergrauen der Zilien und Bemerkungen über den sogenannten plötzlichen Eintritt dieser Veränderung, Klin. Monatsbl. f. Augenh. **44**:228, 1906.

53. Rindfleisch: Ein Fall von einseitgem Ergrauen der Wimpern bei einem Kinde, Klin. Monatsbl. f. Augenh. **40**:53, 1902.

54. Oesterlen, O.: Plötzliches Haarergrauen nach psychischen Insult, Med. Welt **1**:1472, 1927; **5**:1129, 1931.

and Oesterlen stated that no case of sudden whitening of the hair was noted during World War I, sudden poliosis was reported on the basis of first hand medical observation among the Italian air forces.[55]

Bowman [56] stated that "well authenticated instances have occurred in which hair has grown white in a single night, from the sudden influence of some depressing passion." Several well established cases of sudden whitening of hair were reported by Klauder.[57] In 1 of these, a man aged 35 was harassed for a week by the thought that an inexcusable mistake which he had made might result in heavy loss of life aboard a troop ship. He was seen by his associates the night before an official investigation, when no change was noticed in his appearance. The next morning he was shaved by a barber and did not know that his hair had changed color until he arrived at his office, when fellow workers exclaimed, "What is the matter with your hair; it is snow white!"

Landois [58] reported a similar case of rapid whitening of the hair in a man aged 35 who experienced severe terror during delirium tremens. Ornsteen [59] mentioned the case of a woman aged 30 whose hair became entirely white within three hours when she was informed that her child had been run down by a truck. MacLeod [60] described poliosis associated with vitiligo following severe emotional shock. Roose[61] recounted the case of a girl aged 17 whose eyelashes turned white overnight following fright.

Among the cases listed [50] as instances of spontaneous whitening of the hair are several [62] in which only the cilia were involved, and some other pathologic process was present which might involve nerve channels. In other cases, such as that of Rindfleisch,[53] no other complicating factor was disclosed. In my opinion, the nervous origin of poliosis is substantiated by numerous reports of cases of poliosis following trigeminal neuralgia,[63] traumatic wounds,[64] iridocyclitis, nerve injuries [47] and peripheral neuritis [47]; associated with pain in the region innervated by the right trigeminal nerve,[63a] interstitial keratitis and iridocyclitis, [65] and after operations on the eye which were notably painful.[66] In these cases the poliosis was limited to the region of the nerve trunk involved.

Schenkl [5] discovered several silvery white lashes on the temporal half of the left upper lid of a boy aged 9 years, at a time when the eye was sympathetically inflamed in consequence of an injury received by the right eye. On the right upper lid all the lashes were perfectly white except for a minute portion of the tips, which were very dark.

Jacobi [64b] also noted in an eye sympathetically affected with iridocyclitis that the lashes of the nasal half of the upper lid were snow white, while those on the outer half of the same lid were black and white in about equal proportions, the lower lid presenting merely a few white hairs.

That the neurotropic origin of poliosis must be considered in a broader sense is indicated by the cases in which it has occurred after a severe emotional trauma, such as in the case of Hutchinson,[6] the recent case of the complete syndrome reported by Laje Weskamp [19] and the cases of poliosis remarkable for the sudden-

55. Vignolo-Lutati, C.: Canizie precoce e psicopatie di guerra, Policlinico (sez. prat.) **25**:680, 1918.

56. Bowman, W.: The Collected Papers of Sir William Bowman, London, Harrison & Sons, 1892, vol. 1, p. 150; originally published by Todd, R. B., and Bowman, W.: Physiological Anatomy and Physiology of Man, Philadelphia, Blanchard & Lea, 1857, vol. 1, chap. 14, pp. 406-426.

57. Klauder, J. V.: Sudden Whitening of the Hair, After Mental Strain, Arch. Neurol. & Psychiat. **24**: 415 (Aug.) 1930.

58. Landois, L.: Das plötzliche Ergrauen der Haupthaare, Virchows Arch. f. path. Anat. **35**:575-599, 1866.

59. Ornsteen, A. M.: Functional Disorders of the Nervous System as Sequelae to Trauma, Am. J. Surg. **42**:772, 1938.

60. MacLeod, J. M. H.: A Case of Leucodermia and Leucotrichia Following a Motor Accident, Brit. J. Dermat. **49**:437, 1937.

61. Roose: Cas de poliosis ou de canitie des paupières, Ann. Inst. Saint-Antoine (Courtrai), April 1, 1899; abstracted, Ann. d'ocul. **122**:314, 1899.

62. (*a*) de Schweinitz, G. E.: Sudden Turning Gray of the Eyelashes, M. News, Philadelphia **1**:353, 1889; Univ. M. Mag. **1**:353, 1888-1889. (*b*) Hirschberg, J.: Plötzliches Ergrauen von Haupt- (oder Bart-) Haaren, Centralbl. f. prakt. Augenh. **12**:15, 1888.

63. (*a*) Lotin, A.: Ein Fall von einseitigem Ergrauen der Wimpern bei einem Kind, Vestnik oftal., *1902*; abstracted, Ztschr. f. Augenh. **10**:235, 1903. (*b*) Dayus, E. C.: Personal communication to the author. Schreiber.[51]

64. (*a*) Tay, W.: A Case of Symmetrical Whitening of the Eyelashes and Eyebrows in Connection with Sympathetic Ophthalmitis, Tr. Ophth. Soc. U. Kingdom **12**:29, 1891-1892. (*b*) Jacobi, J.: Vorzeitige und acute Entfärbung der Wimpern beschränkt auf die Lider eines sympathisch erkrankten Auges, Klin. Monatsbl. f. Augenh. **12**:153, 1874. (*c*) Nettleship, E.: Remarks on Sympathetic Ophthalmitis with Whitening of the Eyelashes, Tr. Ophth. Soc. U. Kingdom **4**:83, 1884. (*d*) Ponti, F.: Straordinario caso di precoce canizie delle ciglia, Gior. d'oftal. ital. **2**:105, 1859. (*e*) Bach, L.: Traumatische Neurose und Unfallbegutachtung, Ztschr. f. Augenh. **14**:246, 1905. Terrien.[47] Steindorff.[25e] Schreiber.[51] von Michel.[18b]

65. Gasteiger, H.: Ueber frühzeitiges Ergrauen der Cilien, Arch f. Augenh. **95**:261, 1925.

66. (*a*) Reich, M.: Péliose d'origine nerveuse, Arch. d'opht. **1**:307, 1881. (*b*) Luhr, A. F.: Personal communication to the author. Schreiber.[51] von Michel.[18b] Cramer.[14]

ness and rapidity of the change in color. Poliosis following severe emotional trauma has been termed "poliosis neurotica" by Schreiber,[51] and as astute an observer as Hutchinson[6] observed "there can be little or no doubt that these changes are brought about from lesions of the nervous system, and in that relation they are of great interest." Becker[50] asserted that the pathogenesis of poliosis is usually on a functional basis.

As previously stated, the duration of discoloration of the hair varies widely. Vogt[52] stated that in his case of this syndrome depilation of the white hair was followed by regrowth of black hair. In alopecia areata, complicated by regrowth of white hair in the affected areas, the striking piebald appearance may gradually be replaced by a more even distribution of hair pigmentation.

The not uncommon association of poliosis with either alopecia areata or vitiligo is well known. Relevant to consideration of the present case and to the hypothesis advanced is Komoto's[31a] case, in which development of chorioretinal depigmentation was associated with vitiligo and poliosis. That the associated region of the eye may be involved in sudden poliosis is suggested by the case of Roose,[61] in which the eyelashes of the right eye were reported to have turned white overnight after great fright, and by the case of Herzog, cited by Hirschberg,[62b] in which whitening of half the cilia of the right upper lid and some of the eyebrow on the same side occurred in the course of a week.

Medical, particularly dermatologic, opinion holds that poliosis may apparently be spontaneous but that in the main the pathogenesis appears to rest on a neurotropic basis. Other known or possible causes of this condition are circulatory changes, which bring about disturbance in the delivery of pigment,[64c] anaphylactic phenomena[67] and, sometimes, congenital factors.[68] Poliosis and, more commonly, alopecia have followed specific systemic bacterial disease.[52] Tay,[64a] Reich,[66a] and Hirschberg,[62b] all have stated the belief that poliosis is due to nerve influences, and the last-named author suggested that the sympathetic nervous system was involved. It is now well established that neurodermatoses involve dysfunction of the vegetative nervous system.

Poliosis is included among the functional dermatoses by various authorities. Schenkl[5] was the first, in 1873, according to Babel,[4] to observe the appearance of poliosis in association with uveitis, which in his case was of traumatic origin, evidently a true sympathetic ophthalmia. Babel did not mention the equally interesting cases reported by Hutchinson[6] and by Nettleship,[64c] in 1884. Jacobi[64b] reported a case of poliosis similar to that of Schenkl in 1874.

In another, and much earlier, paper Hutchinson[69] asked:

> Is there any reason to believe that in humans, any other nerve than the fifth can either by its irritation or its paralysis, influence the nutrition of the eyeball? Are there any facts which imply that the vaso-motor can produce any other consequences . . . ?

If, in this syndrome, the uveitis (and ocular depigmentation) are, like the alopecia, poliosis and vitiligo, secondary to disease of the hypothalamic vegetative centers, the answer to Hutchinson's question is probably "yes."

Vitiligo.—Vitiligo is a disease of the skin characterized by disappearance of the natural pigment, occurring in patches and leaving whitish areas. According to Becker and Obermayer,[39] it is immediately due to functional derangement of the melanoblasts at the epidermodermal junction. It has been reported in association with poliosis alone,[70] with alopecia,[71] with heterochromia iridis and cataract[32] and with herpes zoster ophthalmicus.[72] In the syndrome under discussion, the process usually involves the region of the brows and may occur on the scalp,[21d] trunk, limbs and genitalia. The fact that its occurrence has not been reported more consistently on the scalp may be due to the fact that the hair has masked its presence. Fluorescing ultraviolet rays bring out the presence of this lesion on the scalp in a striking manner (fig., *A* and *B*). In the case reported here the vitiligo did not appear on the scalp until late in the course of the disease, when the areas of alopecia in this region had been covered with a new growth of white hair. Photographs made with ultraviolet light also show that the vitiligo in this case did not appear simultaneously in the various areas of the skin.

Vitiligo has also been held to occur in the course of prostrating, cachectic disease.[25a] Vitiligo of the eyelids (but not of the brows) has been reported to follow local instillation of a parasympathetic drug.[73]

Although the pathogenesis of vitiligo is not entirely understood, many competent dermatolo-

67. Rones.[11] Cramer.[14]

68. Streatfield, J. F.: Observations on Some Congenital Diseases of the Eye, Lancet **1**:263, 1882.

69. Hutchinson, J.: Suggestions for Further Clinical Work in Ophthalmology, Ophth. Hosp. Rep. 8:1, 1876.

70. MacLeod.[60] Steindorff.[25c] Becker and Obermayer.[39]

71. Becker and Obermayer.[39] Stokes, Beerman and Ingraham.[42]

72. Bauckus and others.[15] Gilbert.[30a] Erdmann.[28a]

73. Corrado, M.: Contributo alla genesi della vitiligine palpebrale consecutive ad istillazione repitute di atropina, Ann. di ottal. e clin. ocul. **60**:914, 1932.

gists regard it as a trophoneurosis or dermatoneurosis.[74] Although Demaria[75] and Gilbert[30a] stated that the vitiligo was an accidental concomitant in their cases, it is striking how completely the vitiligo in the reported cases appeared to be due to the same causes which Genner[43] and Stokes[40] listed for alopecia, viz., peripheral nerve injury, disease of the nervous system and emotional shock. For instance, Steindorff[25e] reported its occurrence after blunt trauma, and Cramer,[14] after a painful operation on the eyes; it has been described in conjunction with Horner's syndrome[76] and as following trigeminal neuralgia[63b] and reference has been made[77] to its association with herpetic states and, of course, with the syndrome under discussion. MacLeod[60] described the association of vitiligo with poliosis following severe emotional trauma. He stated: "It is significant that it [vitiligo] should first have become obvious seven weeks after the accident—a period of time when hair may begin to fall after some serious illness." Hutchinson[78] ascribed localized scleroderma (morphea) to nervous influences.

Reference has been made to the fact that this syndrome in a significant number of cases (especially significant in view of the incompleteness of many of the reports) was preceded either by an "influenzal" encephalitic prodrome or, curiously, by excruciating emotional trauma. In a few cases of this syndrome[79] the various manifestations have shown an atypical relation; their onset has been widely separated in terms of time.

REPORT OF A CASE

History.—A man aged 38, of Italian origin, born in Calabria, Italy, had been working for several months in an oil-tempering room, where steels of various types were treated. About the middle of December 1939 he observed that there were fumes in the tempering room and stated that the vapor irritated his eyes. He complained of this irritation intermittently until about March 19, 1940, when, on returning home, he told his wife that he felt cold and ill. The following day his physician diagnosed his condition as an infection of the upper respiratory tract; during the next few days the illness seemed to resemble influenza, the diagnosis which the physician made. Several days later, before convalescence was complete, the patient noted blurred vision. On the patient's complaining of impaired vision, his physician examined the eyegrounds and recognized elevation of the nerve heads. This observation was confirmed.

For several months the patient had been aware of occasional headaches. These he had attributed to the ocular irritation, which he believed was due to vapors in the room where he worked. After the onset of the infection of the upper respiratory tract the headaches became more severe and more constant and, he stated, were not relieved by medicine which his physician prescribed. He began to be annoyed by ringing in the ears. He complained of a dry, crusting discharge on the eyelids. His wife stated that the patient became lethargic and that it was on this account she became worried about him.

Inquiry into the background of the patient's health revealed nothing significant. There was no history of ocular disease in the family, but examination of his wife revealed an advanced degree of retinitis pigmentosa in each eye.

The patient was admitted to the Buffalo General Hospital on March 29, at the request of the attending physician. There was no elevation in temperature or in the pulse or the respiratory rate. On admission the bulbar conjunctiva of each eye was injected; the ocular media were clear, and there was bilateral papillitis. Physical examination revealed nothing abnormal except for deviation of the nasal septum and pyorrhea.

Laboratory Data.—March 29: Repeated urinalyses revealed nothing except a few white blood cells.

A blood count showed 5,620,000 red cells, a hemoglobin concentration of 113 per cent and 4,450 white cells, with 17 band forms, 71 filiform neutrophils and 12 lymphocytes. A week later the white cell count was 7,600, with 14 band forms, 59 filiform neutrophils, 3 eosinophils, 18 lymphocytes and 6 monocytes. On two occasions the Wassermann reaction of the blood was negative. The dextrose of the blood measured 111 mg.; the urea nitrogen, 13 mg., and the sodium chloride, 467 mg. per hundred cubic centimeters. The sedimentation rates were normal. Bacteriologic examination of a smear of dental material showed fusiform bacilli and spirilla.

April 4: The spinal fluid was clear and colorless; it contained 3 red blood cells and 343 white blood cells per cubic millimeter, with lymphocytes predominating; the reaction for globulin was 1 plus, and that for albumin, 2 plus; there was prompt reduction of copper; the colloidal gold curve was 2222110000. The Wassermann reaction was negative. The protein measured 58 mg., and the chlorides 660 mg., per hundred cubic centimeters.

April 9: The spinal fluid was clear and colorless. Examination revealed 333 white blood cells per cubic millimeter, with lymphocytes predominating, and a trace of albumin and globulin; there was delayed reduction of copper. The protein measured 59 mg., and the dextrose 49 mg., per hundred cubic centimeters. Culture of the fluid yielded Bacillus subtilis; a smear showed no acid-fast bacilli.

April 16: The spinal fluid was clear and colorless. Examination revealed 3 red blood cells and 122 white blood cells, with lymphocytes predominating; a plus-minus reaction was obtained for globulin and a plus reaction for albumin; there was a prompt reduction of

74. Erdmann.[28a] McCarthy.[38] Stokes.[40] Stokes, Beerman and Ingraham.[42]

75. Demaria, E. B.: Consideraciones sobre dos casos de iridociclo-coroiditis doble y grave, en sujetos con vitiligo, Arch. de oftal. hispano-am. **17**:355, 1917.

76. Jonesco-Sisesti; Vasilesco, N., and Palade, G.: Sclérose en plaques avec syndrome de Claude Bernard-Horner et vitiligo, Bull. et mém. Soc. méd. d. hôp. de Paris **53**:941, 1937.

77. Baldino, S.: Irido-coroidite di origine endocrino-simpatica, Arch. di ottal. **27**:244, 1920. Gilbert.[30a] Bauckus and associates.[45]

78. Hutchinson, J.: On Structural Diseases Induced Through the Influence of the Nervous System, Brit. M. J. **2**:915, 1880; Lectures on Clinical Surgery, London, J. & A. Churchill, 1879, p. 338.

79. Babel.[4] Gilbert.[30a] Wexler.[31b] Corrado.[73]

copper, and the colloidal curve was 1111110000; the Wassermann reaction was negative, and the protein measured 150 mg. per hundred cubic centimeters.

April 22: The spinal fluid was slightly cloudy. Examination revealed 21 white blood cells and no red cells, with polymorphonuclear cells predominating. There were a slight trace of globulin and albumin and prompt reduction of copper. The dextrose content was 55 mg. per hundred cubic centimeters. There were no acid-fast bacilli, and inoculation of a guinea pig gave negative results for tuberculosis.

Course of Illness.—Roentgenographic examination during the course of hospitalization showed that the nasal sinuses, gums and teeth were essentially normal, and encephalographic studies gave good visualization of the ventricular system, which appeared to be normal. Continued observation of the fundi revealed, in addition to the bilateral papillitis previously observed, some retinal edema.

On April 13, the clinical impression was that of meningeal reaction, and one neurologic consultant recorded slight paresis of the right sixth nerve. The following day a neurologic consultant gave it as his opinion that there was an inflammatory lesion primarily of the optic nerve and secondarily of the meninges. Gradually the media became more hazy, and anterior uveitis developed in each eye.

Fig. 1.—Photographs of patient (*A*) on July 1, 1940, showing alopecia and developing vitiligo, and (*B*) on Dec. 23, 1940, showing vitiligo and poliosis. Ultraviolet illumination. (*C*) photograph of patient on Dec. 23, 1940, with ordinary incandescent illumination. The vitiligo is less clearly demonstrated than with ultraviolet illumination.

I first saw the patient on June 1, 1940, about two months after the onset of the disease. He stated that about six weeks after the beginning of the loss of vision, he became aware of considerable loss of hair on the scalp. For several weeks, he stated, he found

a good deal of hair on his pillow in the morning. At this time, he said, his brows and lashes began to turn white (fig. 1*A*).

He also complained of partial loss of hearing and of persistent ringing in the ears. He stated that during the first few days of his hospitalization he had a severe headache, which was not relieved at all by medication, and that tinnitus began at that time. During his stay in the hospital, the tinnitus became much less noticeable in the left ear and finally disappeared on that side. He was certain that the headaches and the tinnitus on the left side had stopped three weeks before he left the hospital, on May 20.

Examination.—The patient was well developed. Both eyes showed a moderate degree of injection of the conjunctiva and deep ciliary area. Extraocular muscle balance was normal. Vision in each eye was reduced to light perception and was not improved with glasses. Many keratitic precipitates were dispersed over the entire posterior surface of both corneas. In the left eye the anterior chamber was slightly shallow, the aqueous clear and the margin of the iris entirely adherent to the lens, while in the right eye seclusion of the pupil was nearly, but not quite, complete. The irises were brown and showed some degree of atrophy but no areas of depigmentation. Light projection was present in all directions in both eyes. There was no abnormal interference with transillumination; in fact, transscleral illumination showed pronounced atrophy of the pigment coats of the eyes, with normal density remaining in the region of the ciliary body. There was no corneal hypesthesia. Intraocular tension was 17 mm. (Schiøtz), and in each eye there was a slight degree of tenderness in the ciliary region. The upper and lower lashes of each eye showed partial canities, as did the eyebrows. The skin in the region of the brows showed a clearly delimited loss of pigment. These vitiliginous areas fluoresced rather brilliantly in ultraviolet light, as did several irregular depigmented areas on the skin of the back. Aside from a faint erythema of the margins, there was no sign or evidence of inflammation in or about these areas of leukoderma. The hair of the scalp showed conspicuous patchy areas of baldness, typical of alopecia areata, and these same areas were vitiliginous.

The alopecia also involved the eyebrows and eyelashes, while some of the areas of alopecia on the scalp were completely devoid of hair. Others showed regrowth. The new hairs were somewhat finer and were white. The alopecia of the eyebrows and eyelids was diffuse and not complete. The scalp, the eyebrows and the eyelids showed a diffuse, desquamating, fine dry scale, which had a bright fluorescence with ultraviolet illumination. This scaling was undoubtedly a manifestation of seborrhea. The vitiliginous areas on the back were chiefly in the region of the third and fourth thoracic vertebrae, and there was a faint erythema of the margins. There was no evidence of any inflammatory reaction in this area of leukoderma. None of the lesions were elevated or depressed. Direct microscopic examination and cultures on the Sabouraud medium of scrapings taken from the patches of alopecia and the areas of vitiligo did not reveal the presence of fungi.

On observation with ultraviolet light the vitiligo was much more perceptible. Examination of the nose and throat gave essentially negative results. The ear drums and auditory canals were normal, the eustachian tubes patent and the sinuses clear on transillumination, except for the right antrum, which was clear after irrigation. Audiometric, Weber and caloric tests showed eighth nerve deafness on both sides, not sufficient to destroy all hearing, with functioning labyrinths.

Electroencephalograms did not disclose abnormal potentials. The basal metabolic rate was + 1 per cent.

Progress of the Disease and Present Status.—Progressive changes were limited to the skin, the vitiliginous areas of which showed gradual extension and in which, on the scrotum, violaceous, flat-topped, shiny papules developed, diagnosed as lichen planus; to the hair, with regrowth of white hair in the regions of baldness, producing a striking piebald appearance, and to the eyes, in which the keratitic precipitates became heavier. Later, in October 1942, wheal-like, large papules and bullous lesions developed on the forearms and neck and about the lips; these lesions were diagnosed clinically as erythema multiforme. The tinnitus has persisted "in the right ear." The audiogram taken a year after the first examination showed no change in the partial deafness. Neurologic examinations have revealed nothing significant, although in January 1941 the patient complained of formication, "as though a feather were touching the skin of the head"; by this, he referred to the skin on each side of the head around and above the ears and extending forward to the region of the orbit. This disturbance persisted about ten days. He stated that, beginning about three months after the onset of the illness, he drank more water than previously and that nocturia appeared, micturition averaging once a night. He has noted no change in his appetite for food or loss of libido. There has been no loss of weight.

After operation on the eyes a dense secondary membrane developed in each eye. Iridotomy on the left eye improved vision, with correction, to 20/70 in that eye. No further surgical intervention was attempted on the right eye. The patient has returned to his former occupation. No secondary glaucoma has developed. On the contrary, since operation there has been a varying degree of hypotonicity in the right eye; otherwise it has been quiet and comfortable. At no time has there been evidence of retinal detachment in either eye. Transscleral transillumination shows atrophy of the pigment layers of the eyes, which is now pronounced.

Inoculation Studies.—Using a technic demonstrated to me by Dr. P. K. Olitsky and Dr. Helen Morgan, at the Rockefeller Institute, I gave 4 rabbits intracisternal injections of material from the iris of the right eye, macerated in sterile isotonic solution of sodium chloride. All the rabbits survived. Over a period of six months no organic changes were observed. Three rabbits received similar injections of material from the left eye. Again, no changes were noticed in the skin or the pigmentation of the hair. Two rabbits were killed and sent to Dr. James Papez for examination of the midbrain.

The negative results obtained with animal inoculation at this stage demonstrate the importance of obtaining potentially infected tissue early in the disease, perhaps when the cell count of the spinal fluid is high. It is suggested that cerebrospinal fluid might be used for injection. I should be pleased to cooperate with investigators who have cases of this rare disease under observation and who are not familiar with the rather difficult technic of intracisternal injection into the rabbit.

HYPOTHALAMUS

Anatomic Structure.—The hypothalamus is a name applied to the mamillary bodies, the tuber cinereum and other related structures between the cerebral peduncles and the subthalamic region,[80] which form the floor of the third ventricle. Largely composed of nuclear masses and their tract connections, it is situated just above the hypophysis, below the thalamus and just behind the optic chiasm. Knowledge of the anatomic divisions, the cytoarchitecture, the tract connections and the highly organized, largely vegetative, functions which it integrates is recent for the most part, although Mauthner, an ophthalmologist, ascribed the somnolence associated with encephalitis to an infection of the brain,[81] described engorgement of the walls of the third ventricle and the sylvian aqueduct and, accordingly, conceived of a center for sleep regulation in the hypothalamus. Lesions, such as tumor, in the hypothalamic region produce symptoms simulating those of encephalitis.[82] The patient whose case is reported here appears to have had encephalitis, indicating hypothalamic involvement early in the disease.

The hypothalamic nuclei are numerous, numbering at least fifteen.[81a] To many no specific function has been assigned.[81a] Although commendable attempts have been made [83] to systematize the confusing nomenclature of hypothalamic structure, morphologic relevance in this area is obscure; there appears to be reason to believe that classification of nuclei on the basis of cell type is more illuminating in this area than that based on topographic arrangement.[84]

Embryologically the retina is closely connected with the hypothalamus and the third ventricle.[85] The optic stalks are joined to the part of the first primary cerebral vesicle, from which the hypothalamus is later derived. As Haymaker and his associates [86] pointed out, this relation serves as a clue to the association of pigment changes in the retina with, and he presumed hypothalamic changes in, the Laurence-Moon-Biedl syndrome.

Papez [87] succinctly summarized the close phylogenetic and embryonic relations of the retina, hypothalamus and hypophysis. He made it clear that the apparent complexities of the hypothalamus and its activities can be understood best when considered from the aspect of the numerous structural connections of the region and in the light of its development. While the growth of the hypothalamus is not a uniform, but a differential, process, the development of the optic tracts and the supraoptic decussations seems to be closely related to the origin and growth of the supraoptic nucleus and the anterior hypothalamic area. The development of fibers from the latter and from the supraoptic region occurs early. This fact points to the importance of the hypothalamohypophsial connections, to which I shall refer.

The most anterior portion of the hypothalamus contains the supraoptic, paraventricular and suprachiasmic nuclei, which are connected by fiber tracts with various parts of the hypothalamus, and notably with the hypophysis, the retina and the thalamus. Many of the details of the fiber connections of the hypothalamus have not been worked out; only in recent years [81a] have certain hypothalamic functions been intensively studied, especially in regard to sleep rhythm, control of sympathetic and parasympathetic activity, heat regulation; water, carbohydrate and fat metabolism and sexual pressures.

The evidence that fiber tracts connect the retina and the hypothalamus is now convincing. Haymaker [88] showed, in the dog, a discrete bundle of fibers in the upper lateral part of the optic nerve, slipping away from the optic chiasm and extending to the supraoptic nucleus. Papez [82] has shown me a similar structure in serial sections, an observation which Haymaker [88] regarded as authoritative. Frey [89] claimed to have shown a similar structure in the guinea pig, but

80. Papez, J. W.: Comparative Neurology, New York, Thomas Y. Crowell Company, 1929, p. 297.

81. (*a*) Fulton, J. F.: Physiology of the Nervous System, New York, Oxford University Press, 1938. pp. 223-253. (*b*) Lebensohn, J. E.: The Eye and Sleep, Arch. Ophth. **25**:401 (March) 1941.

82. Papez, J. W.: Personal communication to the author.

83. (*a*) Clark, W. E. L.; Beattie, J.; Riddoch, G., and Dott, N. M.: The Hypothalamus, Edinburgh, Oliver & Boyd, Ltd., 1938. (*b*) Rioch, D. M.; Wislocki, G. B., and O'Leary, J. L.: A Précis of Preoptic, Hypothalamic and Hypophysial Terminology with Atlas, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:3, 1940.

84. Morgan, L. O.: Cell Changes in Hypothalamus in the Major Psychoses, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:753, 1940.

85. Ryder, J. A.: Development of the Eye, in Norris, W. F., and Oliver, C. A.: System of Diseases of the Eye, Philadelphia, J. B. Lippincott Company, 1897.

86. (*a*) Haymaker, W., and Saunders, J. B. de C. M.: Hypothalamus: Present Conception, Internat. Clin. **2**: 226, 1940. (*b*) Haymaker, W., and Anderson, E.: Hypothalamus: Functions and Clinical Syndromes of the Hypothalamus, ibid. **2**:253, 1940.

87. Papez, J. W.: The Embryologic Development of the Hypothalamic Area in Mammals, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:31, 1940.

88. Haymaker, W.: Personal communication to the author.

89. Frey, E.: Studien über die hypothalamische Optikuswurzel der Amphibien, Proc. Sect. Sc. Roy. Acad. Sc., Amsterdam **41**:1004, 1938.

it is possible that he saw only aberrent fibers of the optic decussation.

As early as 1931, Greving,[90] whose anatomic description of the hypothalamic nuclei Fulton found most satisfactory, observed in the human brain a contingent of fibers escaping from the optic chiasm (derived presumably from the retina), to enter the hypothalamus and pervade the supraoptic nucleus. These retinal-hypothalamic connections are not to be regarded[88] as identical with aberrent fibers of the optic decussation, described by Jefferson[91] in the ferret. According to Frey,[92] the hypothalamic root of the optic nerve is highly developed in man. Marburg[93] corroborated this statement.

Similarly, the existence is now accepted[94] of hypothalamohypophysial fibers, functionally related to retinal-hypothalamic tracts and forming with them (to view the matter simply) retinal-hypophysial connections. The same supraoptic nucleus previously referred to as the terminus of the retinal fibers gives rise[81a] to the supraopticohypophysial tract, which terminates in the pars intermedia and the pars posterior of the pituitary. Other hypothalamohypophysial connections are said to involve the paraventricular nucleus, of the hypothalamus,[81a] the median eminence and the pars tuberalis, of the pituitary. Diencephalohypophysial connections were described in the fish by Ariëns Kappers[95] as early as 1906, and the evidence for the existence of similar tracts in other species was reviewed by Scharrer,[94] Haymaker and Saunders[86] and Clark and associates.[83a]

Functional Evidence of Retinohypothalamohypophysial Relations.—It is well known that the melanophore hormone of the pituitary will cause "pigment migration," or expansion of the melanophores, in the skin of the frog, which becomes dark. Frogs without a hypophysis do not change color, as do normal frogs when moved from a light to a dark room, or vice versa. Furthermore, no melanophore hormone is found in the hypophysial extract of the frog killed after it has remained in darkness twenty minutes; but if the donor frog is allowed to remain a few seconds in daylight, light stimuli from the eye activate the hypophysis, and an extract prepared from its hypophysis will produce darkening of the skin of the frog given the injection. It has also been shown[96] that the melanophore hormone is increased in the blood stream of human subjects and of rabbits during the night.

That there is a remarkably close functional association of the hypothalamus and the hypophysis is indicated by the experiments of Cushing and Clark and associates,[83a] showing that hypothalamic function is stimulated by a pituitary secretion, which may be carried to the hypothalamus not only by the blood stream but by a hypophysial colloid secreted directly into the third ventricle, adjacent to the hypothalamus. The embryonic relations of the anterior hypothalamus, hypophysis, retina, optic tracts and supraoptic decussations (including Gudden's commissure) have been previously indicated.[87] Functionally there is a relation of the retina, via the optic tracts, the hypothalamus and the activity of the pituitary, as shown by experimental work on amphibians,[89] hens[97] and other vertebrates.[98]

There is much evidence to indicate that gonadal activity and genital development are influenced when the optic nerve is stimulated. It is widely known that egg production is increased when the hen house is illuminated at night; equally effective is pinching the optic nerve.[94] Rodewald[99] showed that visual or mechanical stimulation affected the testicular structure of male ducks, and this relation of retinal to pituitary activity has been confirmed by the work of other investigators and reviewed recently by Haymaker and Saunders,[86] whose attention it has not escaped that light is effective in stimulating gonadal activity in wild animals and in man. The effect of the light stimulus on sexual cycles and on dermatoneuroses, as well as on basic ethnologic factors, was reviewed in 1916 by Woodruff in a comprehensive monograph.[100] More re-

90. Greving, R.: Die vegetative Zentren im Swischenhirn, in Müller, L. R.: Lebensnerven und Lebenstriefe, Berlin, Julius Springer, 1931, p. 115.

91. Jefferson, J. W.: A Study of the Subcortical Connections of the Optic Tract System of the Ferret, with Special Reference to Gonadal Activation by Retinal Stimulation, J. Anat. **75**:106, 1940.

92. Frey, E.: Vergleichend-anatomische Untersuchungen über die basale optische Würzel, usw., Schweiz. Arch. f. Neurol. u. Psychiat. **39**:255, 1937.

93. Marburg, O.: Personal communication to the author.

94. Scharrer, E.: Ueber ein Vegetatives optisches System, Klin. Wchnschr. **16**:1521, 1937. Lebensohn.[81b] Haymaker.[88]

95. Ariëns Kappers, C. U.: The Structure of the Teleostan and Selachian Brain, J. Comp. Neurol. **16**:1, 1906.

96. Jores, A.: Melanophorenhormon und Auge, Klin. Wchnschr. **12**:1599, 1933; cited by Scharrer.[94] Greving.[90]

97. Morgan, L. O.: Personal communication to the author.

98. Clark, W. E. L.; McKeown, T., and Zuckerman, S.: Visual Pathways Concerned in Gonadal Stimulation in Ferrets, Proc. Roy. Soc., London, s.B **126**:449, 1939.

99. Rodewald, W.: Die Wirkung des Lichtes auf die Hypophyse von Rana tempororia L., Ztschr. f. Vergl. Physiol. **21**:767, 1935; cited by Scharrer.[94]

100. Woodruff, C. E.: The Effects of Tropical Light on White Men, New York, Rebman Company, 1916.

cently, Sanchez-Calvo [101] has shown that rabbits and guinea pigs exposed to darkness for as short a period as three days show cellular changes in the hypophysis. In man, also, sexual activity is affected by *stimulation with light*. As Haymaker and associates [86] pointed out, it is generally recognized that the people of a southern climate reach sexual maturity earlier than do northern races. Llewellyn [102] stated that during the long polar night, Eskimo women neither menstruate nor conceive, and Woodruff [100] stated that the return of spring brings what really amounts to a rutting season among these people. There is a good deal of evidence to support the contention that light, rather than other climatic factors, principally affects the sexual cycles in mammals. Much of the evidence was summarized by Woodruff,[100] who also stated that light influences the fattening of cattle (and of human beings). It will be recalled that fat metabolism is influenced by the hypothalamus.

Many investigators have used the technics of ablation, tract section and excitation to study hypothalamic activity in general, including the role which visual impulses play in gonadal activity. Ablation and tract section technics do not allow close comparison with the more subtle effects, involving both depression and excitation of function, which are presumably produced by the hypothalamic lesions of disease. The defects of excitation technics have been analyzed by Fulton.[81a] Recently the view was expressed [103] that visually generated impulses pass via the optic pathway and the supraoptic and tuberal nuclei of the hypothalamus, and thence via the supraopticohypophysial and tuberohypophysial tracts of the anterior lobe of the hypophysis, or to the pars intermedia and the pars posterior.[81a] Haymaker [88] also stated:

> Another possible reflex pathway from retina to hypophysis is via accessory optic tracts to the subthalamus and thence via the fasciculus tuberis descendens to the tuber cinereum, where a relay enters the neurohypophysis.

Roussy and Mosinger [104] stated that hypothalamosensory fibers include retinal connections which can be demonstrated in man—that these fibers probably regulate the excitability of the retina (the question of cerebral influences on dark adaptation arises) and may supply trophic innervation to the retina and choroid. They suggested that these connections explain structurally the relative frequency (referred to from the embryologic standpoint in a preceding paragraph with which retinosis pigmentosa is associated with hypothalamic lesions, e. g., the Laurence-Moon-Biedl syndrome.

A considered opinion probably will hold [105] that it is all too easy, on the basis of theoretic consideration, to ascribe unprovable functions to tenuously defined tracts in the hypothalamus, to diencephalic nuclei which are topographically diffuse and possibly more easily classified in terms of cell type. It is probably well to remember that, as Clark stated, the hypothalamus is phylogenetically one of the most ancient parts of the vertebrate forebrain; and it may well be, as Riley suggested, that even some of the tracts discernible in man are vestigial and of little functional importance. But the fact that the hypothalamus does show alteration in cases of various systemic diseases in which there has been opportunity to examine it [84] and that the morbid processes known to involve the hypothalamus, as well as experimental lesions in this area, cause a wide variety of systemic manifestations serve to emphasize the exceedingly active role the hypothalamus plays in the hierarchy of the vegetative nervous system.

Justification for my proposing the hypothesis presented in this paper, without, at present, much substantiation based on human material or animal experimentation, may be found in the following facts:

1. The disease is rare, and unless the greatest possible utilization is made of all human material as it becomes available, answers to these important questions may long be postponed.

2. The disease is obviously not one that lends itself readily to experimentation on living human subjects.

3. There is reason to believe that it may be possible to transmit the causative agent of the disease, presumably a virus, to certain experimental animals. Such transmission is not easily accomplished, in view of the rarity of the disease, and since the infective material must be obtained from the spinal canal or from intraocular tissue of infected subjects, the need to conserve the small amount of tissue available for this purpose is readily apparent.

101. Sanchez-Calvo, R.: Einfluss der Dunkelheit auf das Zellbild der Hypophyse, Virchows Arch. f. path. Anat. **300**:560, 1937.

102. Llewellyn, L. J.: Light and Sexual Periodicity, Nature, London **129**:868, 1932.

103. Cahane, M., and Cahane, T.: Sur certaines modifications de l'hypophyse après une lésion du centre infundibulaire régulateur de la function génitale, Rev. franç. d'endocrinol. **13**:366, 1935; Sur certaines modifications des glandes endocrines après une lésion diencephalique, ibid. **14**:472, 1936; cited by Haymaker and Anderson.[86b]

104. Roussy, G., and Mosinger, M.: L'hypothalamus chez l'homme et chez le chien, Rev. neurol. **63**:1, 1935.

105. Riley, H. A.: Epidemic Encephalitis, Arch. Neurol. & Psychiat. **24**:574 (Sept.) 1930. Penfield, W.: Diencephalic Autonomic Epilepsy, Arch. Neurol. & Psychiat. **22**:358 (Aug.) 1929.

Shortly after the patient whose case is reported here came under my observation, it occurred to me that there might be some way of accounting for the bizarre and striking manifestations of this syndrome in terms of a discrete lesion. It would be surprising if a case of this sort did not incite speculation regarding the pathogenesis of the syndrome. The rather definite encephalitic prodrome must suggest a basal intracranial lesion; and consideration of the material reviewed in the fields of morphologic and functional neurology, and of certain provocative concepts in neurodermatology advanced by Stokes, Beerman and Ingraham,[42] leads me directly to the conclusion that a lesion in the suprachiasmatic region of the hypothalamus, and only that one lesion, would account for the entire syndrome, including prodromal encephalitis (usually present), uveitis, certain dermatoneuroses, dysacousia and, sometimes, pronounced cryesthesia. I brought the matter before Dr. James Papez, who corroborated my suggestion and put me into touch with recent authoritative work in this field.

Heersema [106] stated that the symptoms of initial encephalitis include headache, mild fever and general malaise, somnolence or disturbance in sleep rhythm, visual disturbances, choreiform movements, and even paralytic symptoms of the extremities. It is well known that these features may subside on recovery of the patient from the acute stage, and it may be difficult to obtain a significant history when one is attempting to establish evidence to explain the appearance of encephalitic sequelae months or years later, especially in the absence of any epidemic.

Fulton [81a] quoted, and apparently accepted, the statement of von Economo [107] and that of Eaves and Croll [108] that the hypothalamus is invariably involved in encephalitis lethargica. In this disease the disturbance of sleep rhythm is referred by most authorities to the hypothalamus.[80] This symptom was pronounced in the present case, as in other cases of the syndrome under discussion. The cryesthesia mentioned in the reports of several cases of the syndrome also points to this region of the brain.[109] Dott and associates [83a] cited a case in which a man with a large intrasellar cyst became subject to hot sweats and sensitive to cold and constantly felt so cold that he wore socks and required hot water bottles in bed, even in warm weather. This case bears a striking similarity to that of a patient with the syndrome of oculocutaneous pigmentosis, reported by Avalos,[21d] who experienced severe cryesthesia. The fact that the thermal disturbances were largely subjective, as far as one can tell from the reports, suggests that tracts known to connect the hypothalamus with the thalamus,[110] or the thalamus itself, may have been involved.

Hyperglycemia, reported in 1 case of this syndrome,[24] was attributed by the observer to hypophysial derangement. The hypocholesteremia in the same case might fit in with the concept of a hypothalamic lesion, since there is sufficient reason to believe that the role of the hypothalamus in the regulation of fat metabolism is closely associated with its influence on the metabolism of carbohydrates.[81a]

Although the comprehensive reviews of hypothalmic correlations of Grinker, Ingram and Ranson,[111] and the definitive monograph of Clark and associates [83a] on the hypothalamus do not mention a single cutaneous expression of disturbance of this region, Stokes [40] was impressed by reports of "extraordinary seborrheic activity with accompanying dermatitis observed in cases of encephalitis." It is conceivable, Papez [82] agreed, that fibers from the supraoptic region to the pars intermedia of the hypophysis may mediate the alopecia areata, poliosis and vitiligo observed in this syndrome. Morgan [97] concurred in this opinion; he expressed the belief that the changes in pigment in the pigmentary layer of the eye and in the skin may be ascribed to a lesion in the suprachiasmic gray matter of the hypothalamus. Marburg [93] would seem to agree; he found that hypothalamic influence on sudden change in color in lower animals is direct but that hormonal and vegetative mechanism are involved in the more highly developed organisms. The role which the hypothalamus plays in organic disturbances precipitated by dysfunction of the vegetative nervous system, as Fulton pointed out,[81a] was not recognized until attention was recently focused on the possibility that such

106. Heersema, P. H.: Symposium on Present State of Endocrine Therapy, M. Clin. North America, 1940, p. 1181.

107. von Economo, C.: Encephalitis Lethargica: Its Sequelae and Treatment, translated by K. O. Newman, New York, Oxford University Press, 1931.

108. Eaves, E. D., and Croll, M. M.: Pituitary and Hypothalamic Region in Chronic Epidemic Encephalitis, Brain **53**:56, 1930.

109. Ziegler, L. H., and Cash, P. T.: A Study of the Influence of Emotions and Affects on the Surface Temperature of the Human Body, Am. J. Psychiat. **95**:677, 1938. Fulton.[81a]

110. Rioch, D. M.: Studies on the Diencephalon of Carnivore: III. Certain Myelinated-Fibre Connections of the Diencephalon of the Dog, Cat, and Aevisa, J. Comp. Neurol. **53**:319, 1931.

111. Grinker, R. R.: Hypothalamic Functions in Psychosomatic Interrelations, Psychosom. Med. **1**:19, 1939. Ingram, W. R.: The Hypothalamus: A Review of the Experimental Data, ibid. **1**:48, 1939. Ranson, S. W.: Note with Regard to Temperature Regulation, ibid. **1**:92, 1939.

changes might involve hypothalamic centers, and the necessary tissue studies were carried out. He referred specifically to the effects of hypothalamic lesions on the gastrointestinal tract. In cases of pellagra, in which dermal manifestations, including pigmentation, are characteristic, degenerative changes have been described in the hypothalamic nuclei, and Vonderahe,[21b] who tentatively accepted these reports, called attention in this connection to Rassulev's [112] observation that about 25 per cent of the patients with pellagra present symptoms of mild diabetes insipidus, the causative lesion of which is known to involve primarily the supraoptic nuclei.

That a lesion in this area of the hypothalamus may cause alopecia, poliosis and vitiligo is evidenced by the case reported by Vonderahe and Abrams [113] of a man aged 40; there were, in addition to evidence of an expanding intracranial lesion, definite changes in the color of the skin, especially around the eyes, alopecia and rapid graying of the hair of the head, as well as nocturia and polyuria. It is now well established that the hypothalamus controls water metabolism and that diabetes insipidus is essentially a hypothalamic derangement, involving especially [83a] the supraoptic nucleus previously referred to. Their patient complained of impotence, which is, as Riddoch [83a] stated, a hypothalamic symptom. In this case, too, as in most of the reported cases of the syndrome under discussion, there was dysacousia, which consisted of buzzing and ringing in the ears and definite impairment of hearing in the left ear. The skin changed color (darkened), especially around the eyes. There was an increasing tendency toward lethargy. Autopsy showed an ependymoma of the third ventricle, distending especially its left wall, impinging on the hypothalamus and destroying the mamillary bodies. The fiber pathways in the corpus callosum immediately superior to the third ventricle presented extensive degenerative changes, evidently an effect of pressure. The columns of the fornix in the roof of the third ventricle were similarly affected. There was notable loss of cells in the thalamus. The fiber tracts of the internal capsule on each side showed loss of myelin. The anterior commissure was involved by the tumor. The globus pallidus showed loss of cells. The optic chiasm was directly invaded by the tumor. The tuber cinereum was completely replaced by neoplastic growth.

Plummer and Jaeger [114] described pigment changes in a young man in whom a glioblastoma had invaded the tuber cinereum and the right hypothalamic region. He was dark of complexion; but his skin grew lighter, and the hair of the beard, lashes, brows and axillary and pubic regions became first lighter and then sparse. Polyuria and fatigability were noted.

Laje Weskamp [19] attributed the dysacousia in his case of the syndrome to disturbance of the vegetative nervous system, specifically of the carotid plexus or the petrous nerve. It is held [82] that the supraoptic decussation of Gudden carries fibers connecting the dorsal anterior parts of the medial geniculate bodies. Clark and his associates [83a] stated that fibers in Gudden's commissure can be traced on each side back to the medial geniculate bodies and that it is possible that some fibers extend to the inferior colliculus (quadrigeminal body), and perhaps to the nucleus of the lateral lemniscus. One may conclude that this commissure is an integral part of the auditory system of the forebrain. Involvement of this structure in pathologic processes affecting adjacent areas might account for the dysacousia both in cases of this syndrome and in the case of Vonderahe and Abrahams [113] (see also the case of Hamby and Gardner [115] of ependymal cysts with bilateral deafness and figure 2).

There remains only the question of the possible relation of a hypothalamic lesion to the uveitis. Evidence is ample that retinohypothalamic nerve tracts exist in man,[93] as well as in animals.[94] On the basis of investigations with experimental animals, largely in the field of animal husbandry, it appears probable that at least some of these fibers are afferent; but, as has previously been pointed out, Roussy and Mosinger [101] described an efferent pathway to the retina, from the tangential nucleus (nucleus supraopticus), which probably regulates the excitability of the retina and possibly supplies trophic innervation to the retina and the choroid. They suggested that this trophic innervation may exert a controlling influence on deposition of the retinal pigment, and in this way explain the relative frequency of the association of retinal pigmentation with a disease in which hypothalamic involvement is suspected, namely, the Laurence-Moon-Biedl syndrome.

There is also reason to believe that a pathway exists not only from the retina to the supra-

112. Rassulev, J. A.: Ueber Diabetes insipidus bei Pellagra, Arch. f. Schiffs- u. Tropen- Hyg. **36**:481, 1932.

113. Vonderahe, A. R., and Abrams, N. R.: Ependymoma of the Third Ventricle, Arch. Ophth. **12**:693 (Nov.) 1934.

114. Plummer, D. E., and Jaeger, J. R.: Pituitary Cachexia (Simmond's Disease): Report of a Case with Autopsy, Arch. Neurol. & Psychiat. **40**:1013 (Nov.) 1938.

115. Hamby, W. B., and Gardner, W. J.: An Ependymal Cyst in the Quadrigeminal Region, Arch. Ophth. **57**:393, 1928.

chiasmic nucleus but thence, by way of the infundibulum, to the pituitary,[116] and it appears possible that pigmentary changes in the eyes, as well as in the skin and hair, may have their pathogenesis in the suprachiasmic gray matter of the hypothalamus. As early as 1911 Erdmann [28a] commented on the association of dermal vitiligo with depigmentation of the ocular fundus and suggested that depigmentation of the retina, or of the iris, may in a sense be a trophic neurosis. He also pointed out the relation of "ocular vitiligo" to herpetic disease and asserted that vitiligo and uveitis may have a common origin. Since herpetic disease of the eye is certainly due to virus infection, discussion, later, of the probable virus nature of this syndrome is justified. Baldino [77] described a case of vitiligo of the skin, the eyelids and the iris, following herpetic iritis, and Gilbert [30a] stated that depigmentation of the ocular fundus and that of the skin and hair are comparable. In cases of this syndrome, when

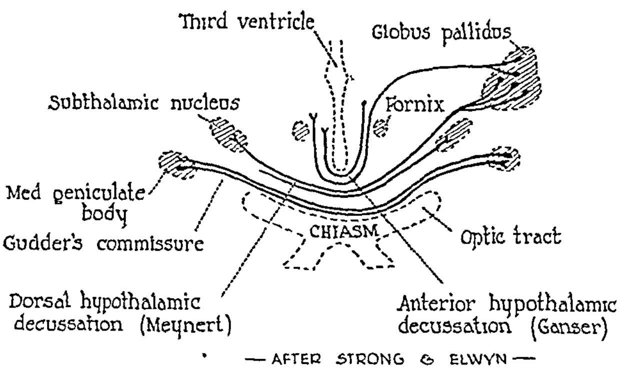

Fig. 2.—Relations of the commissure of Gudden (after Bailey, F. R.; Elwyn, A., and Strong, O. S.: Bailey's Text Book of Histology, ed. 9, Baltimore, William Wood & Company, 1936).

opacification of the media has not obscured the fundus, a striking depigmentation has been observed [31a,b]

Komoto [31a] was the first to describe vitiligo of the fundus as a part of the syndrome. He noted that the poliosis and dermal vitiligo occurred at about the same time and suggested that the absorption of pigment in the two structures had a common cause. Whatever may be the nervous mechanism involved in all the pigment changes in this disease, it is probable that they are closely related. It is well known that the pars intermedia of the hypophysis exerts control of pigmentation in the body, and to me it seems possible that a lesion involving the fiber tract from the supraoptic region to the hypophysis produces the alopecia areata, the poliosis and the dermal vitiligo and that the profound disturbances of the pigment structures in the eye may be responsible for the severe inflammatory process which follows, somewhat as a melanotic sarcoma of the choroid may produce intraocular inflammation, even that closely resembling, if not identical with, sympathetic ophthalmia.

The reasons for the belief that the hypothalamus is implicated in this syndrome may be summarized as follows:

1. Clinical evidence presented by this syndrome of oculocutaneous pigmentosis points to early involvement of the hypothalamus.

2. The posterior segment of the eyeball is closely related structurally, embryologically and phylogenetically to the hypothalamus.

3. Functional considerations point to retinohypothalamic relations.

4. A lesion in the region of the supraoptic-suprachiasmic nuclei of the hypothalamus would, in a very small area, involve or impinge on centers and tracts which, on the basis of considerable evidence, control or affect pigmentation of the eyes, hair and skin, as well as hearing.

5. Hypothalamic involvement accounts for the lethargy and cryesthesia which some of these patients experience.

6. Only one lesion, and that in the suprachiasmic region, can account for all the symptoms of this syndrome.[108]

In summary, then, it may be said that anatomic and physiologic facts substantiate the existence of a vegetative optic system and that the evidence does not conclusively demonstrate that all the fibers are strictly afferent. The existence of these tracts, in fact, recalls a question which, in 1876, Jonathan Hutchinson [69] asked future investigators to consider: "Is there any reason to believe that in humans, any other nerve than the fifth can, either by its irritation or its paralysis, influence the nutrition of the eyeball?" Does it appear less credible that pronounced changes in pigment deposit in the eye may be subject to control by the autonomic nerve system than that such nerve control exists with respect to the skin and hair? The evidence that poliosis and vitiligo are dermatoneuroses has been shown to be more than suggestive. The pronounced "whitening" of the ocular fundus in cases of Harada's disease.[31b] and in certain cases of this syndrome points to such a parallelism.

VIRUS

The frequency with which cases of this syndrome are immediately preceded by an influenza-like episode of encephalitis has previously been mentioned. That "influenza" and certain forms of encephalitis are due to virus infection is now common medical knowledge.

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116. Rasmussen, A. T.: Effects of Hypophysectomy and Hypophyseal Stalk Resection on the Hypothalamic Nuclei of Animals and Man, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:245, 1940.

Workers in the field of virus disease [117] contend that certain neurotropic viruses may pass along the nerve pathways connected with the hypothalamus and that they tend to localize in the latter region and there to produce local necrosis, just as in the exanthems focal multiplication of virus occurs in the skin. The occasional association of certain of the manifestations of this syndrome with herpetic disease, previously indicated, suggests a virus origin. Baldino [77] reported a case of vitiligo of the skin of the eyelid and of the iris following herpes of the iris. Davies,[12] in his stimulating résumé of the syndrome, asserted that the herpes virus is a dermoneurotrope and that it may give rise to this form of vitiligo by causing an intraocular inflammation, similar to sympathetic ophthalmia. Bung, in comment on these cases, suggested that the herpes virus is the etiologic agent. As early as 1890, Bock [18a] ascribed inflammatory lesions of ocular structures following influenza to the "virus of influenza." The same author, in an excellent review of the syndrome, called attention to the hypothesis that recurrent iritis with hypopyon associated with an aphthous infection of the genital organs and buccal patches may be due to a virus. There may be some relevance in the case of Noyes, cited by Mauthner,[1b] in which herpes zoster ophthalmicus was followed by destructive uveitis in the left eye and, ten months later, by a similar severe inflammatory process in the previously intact right eye. Jeffries [1b] noted temporary sympathetic disturbance in the fellow of an eye affected with herpes zoster. The striking resemblance of this syndrome to Harada's disease has been commented on by Magitot and Dubois-Poulsen [21e] and by Takahashi.[118] The outstanding features of Harada's disease are the prodrome of general malaise, followed by bilateral uveitis, often with relatively slight involvement of the anterior segment, by diffuse neuroretinitis and, then, by extensive bilateral detachment of the retina; in view of the pronounced intraocular changes, vision after recovery may be surprisingly good. Bilateral detachment of the retina does not occur, however, in the syndrome under discussion, as reported by Laje Weskamp,[19] Arisawa,[119] and Koyanagi.[8] Magitot and Dubois-Poulsen [21e] reported a case showing most of the symptoms of each syndrome. The spinal fluid exhibited marked pleocytosis, comparable to that in my case and in 4 of Takahashi's [118] 6 cases. Magitot and Dubois-Poulsen [21e] concluded that the causative agent in their case was probably a neurotropic virus. They admitted that an epidemic has never been observed, but Schiff-Wertheimer,[120] in discussing the point, mentioned several cases, not completely typical, occurring in a small French village. Laje Weskamp [19] critically appraised the theory that the causative agent is a neurotropic virus and predicted that this hypothesis would find more supporters.

In several respects the similarity of this condition to sympathetic ophthalmia deserves notice. Hutchinson,[6] in a report of historical interest, described an incomplete case of this syndrome as one of "non-traumatic sympathetic ophthalmia." Laje Weskamp [19] and Soriano [21f] pointed out that one manifestation of the syndrome, dysacousia, is sporadically encountered in sympathetic ophthalmia. When it occurred in the latter condition, Komoto [31a] referred to it as sympathetic deafness. Laje Weskamp [19] stated that Peter, who wrote extensively on sympathetic ophthalmia, had expressed agreement with this view. Laje Weskamp [19] stated the belief that poliosis occurs occasionally with sympathetic ophthalmia, and Nettleship [64c] reported the occurrence of poliosis in the course of traumatic sympathetic ophthalmia. Takahashi [118] was struck by the resemblance of this condition both to Harada's disease and to sympathetic ophthalmia. The histologic resemblance of this condition to sympathetic ophthalmia was especially apparent in 1 of 3 eyes microscopically examined.[121] Ogawa,[122] who was cited by Knapp in an abstract of his article, pointed out that the microscopic picture presented by sympathetic ophthalmia is sometimes atypical. The work tending to support the view that this condition is caused by a virus has been partially summarized by Duke-Elder [1a] and includes the positive results obtained in animals with herpes virus by Gifford and Lucic.[123] Although the histologic changes in their animals less closely resembled those of sympathetic ophthalmia than did the clinical picture, the microscopic discrepancy may

117. Sabin, A. B., and Olitsky, P. K.: Influence of Host Factors on Neurosinvasiveness of Vesicular Stomatitis Virus, J. Exper. Med. **66**:15, 1937; **67**:210, 1938.

118. Takahashi, M.: Klinische und experimentelle Studien über das Wesen von sog. idiopathischer doppelseitiger schwerer Uveitis, Acta Soc. ophth. jap. **34**:506, 1930.

119. Arisawa cited by Koyanagi.[8]

120. Schiff-Wertheimer, in discussion on Magitot and Dubois-Paulsen,[21e] p. 227.

121. Jacobi,[64b] in a case of sympathetic ophthalmia, was the first to examine microscopically an eye clinically associated with poliosis of the cilia.

122. Ogawa: Pathology of the So-Called Idiopathic Uveitis with Dysacousia and Poliosis, Acta Soc. ophth. jap. **38**:68, 1934; abstracted, Arch. Ophth. **13**:1089 (June) 1935.

123. Gifford, S. R., and Lucic, L. H.: Sympathetic Uveitis Caused by the Virus of Herpes Simplex, J. A. M. A. **88**:465 (Feb. 12) 1927.

well have been due to the variation in cellular response in different species. Further work demonstrating that either sympathetic ophthalmia or this syndrome is caused by a virus might be construed as throwing light on the etiologic agents of both conditions.

Takahashi [118] injected liquid vitreous from several patients with this syndrome into the cisterna of rabbits. In 2 of the 5 animals receiving such injections optic neuritis and uveitis developed. He also injected cerebrospinal fluid from his patients into the vitreous of rabbit eyes and in a few instances produced uveitis. Experimental transmission from rabbit to rabbit gave positive results. Intracerebral injections in rabbits produced no clinical change. He followed his animals for several months, and even after intraocular injections a slight initial inflammatory reaction was transient enough to be separated by a distinct time interval from the severe uveitis which ultimately developed. In connection with work of this sort, it is helpful, however, to remember that experimental transmission of virus disease is difficult to interpret, and Olitsky [124] stated that accidental contamination of material accounted for some of the positive results reported in this field. Frequently, moreover, virus material will not "take" at first, and it may be necessary to give the animal an injection every three or four days, until a "take" is secured.[125]

Malbrán and Muhlmann [25a] injected vitreous from a patient with Harada's disease into the subarachnoid space of rabbits and reproduced the uveitis and optic neuritis. They also injected spinal fluid from their patient into the vitreous of rabbits and produced intraocular inflammation which, twelve to sixteen days later, appeared in the untreated eye. They ascribed their positive results to a neurotropic virus "similar to the causative organism of herpes or sympathetic ophthalmia."

It is clear that confirmation of this experimental work will be of great importance in the elucidation of the cause of this syndrome, and possibly of sympathetic ophthalmia. Partial justification for the presentation of a speculative paper on this subject lies in the hope that it will lead to the utilization of clinical material as it becomes available.

In the case recently reported by Givner,[126] technics for virus study were employed only with aqueous and iris material, and only more than a year after the prodromal stage.

124. Olitsky, P. K.: Personal communication to the author.

125. Toomey, J. A.: Personal communication to the author.

126. Givner, I.: Bilateral Uveitis, Poliosis and Retinal Detachment with Recovery, Arch. Ophth. **30**: 331 (Sept.) 1943.

SUMMARY

In the case reported here, as in other cases of the syndrome, transient encephalitis, the presence of which was proved by examination of the cerebrospinal fluid, was preceded by a sense of superficial irritation of the eyes and general malaise, was accompanied by severe cephalalgia, tinnitus, lethargy, optic neuritis and transient unilateral palsy of the sixth nerve and was followed by nerve deafness, severe bilateral uveitis and certain dermatoneuroses. Vitiliginous areas were observed to fluoresce in ultraviolet light. Later, the patient complained of transient paresthesia and of polyuria.

Evidence that alopecia areata, vitiligo and poliosis are neurodermatoses led to the suggestion that, in the same sense, the intraocular reaction, in which disturbance of ocular pigment is notably prominent, is a neurochoroidosis and that a hypothalamic lesion, the result of encephalitis, might affect retinohypothalamicohypophysial vegetative fibers, possibly neurotropic and afferent to hormonal effectors, and so related to control of pigmentary states. Since it is known that the hypothalamus mediates or regulates certain subcortical levels of consciousness, it appears relevant to the hypothesis that in a case in which prodromal encephalitis was not in evidence the condition was known to follow unusually severe emotional trauma. Further confirmation is found in a case of tumor of the third ventricle, pressing on the hypothalamus, in which practically all these manfestations were noted, including dysacousia, which the authors concluded was adventitious in their case.

Interplay between emotion and infection, and between allergy and vasomotor mechanisms, is known to exist, and cases have been observed in which the neurodermatoses previously mentioned occurred alone and followed intense emotional activity.

Certain other hypothalamic functions appear to be involved in this syndrome.

This disease complex shows similarity to sympathetic ophthalmia with respect to symptoms, including possible dysacousia, and to histologic features, and the evidence exists that either or both may be due to virus infection. Although cisternal inoculation of experimental rabbits did not reproduce the disease in this case, it is known that repeated inoculations of virus materials is frequently necessary to obtain a "take." Further work in other laboratories tending to demonstrate a virus origin is justified.

454 Franklin Street.

Clinical Notes

AUTOINOCULATION OF THE EYELIDS WITH VACCINIA

W. R. KLUNZINGER, M.D., ANN ARBOR, MICH.

Although ocular complications following vaccination are not rare, they are uncommon, and it is thought timely to call attention to the omnipresent possibility of their occurrence.

Their mode of occurrence may be of two types: autoinoculation, in which there is direct transfer of the virus from the site of vaccination to the eyes; and heteroinoculation, in which the virus is transferred from one person to another.

The lids, conjunctiva or cornea may be involved; of these, involvement of the cornea is most serious, since in this type impairment of vision may result. In approximately one third of the reported cases of vaccinia with ocular complications the cornea has been involved.[1]

Appearance of the patient in a case of autoinoculation of the eyelids following vaccination for smallpox.

REPORT OF A CASE

G. B., an 8 year old white boy, was first seen on May 5, 1943. One week before he had been vaccinated on the right arm. Three days after the vaccination the patient noted redness and swelling of the lids of both eyes. The condition of the lids became progressively worse. At the time the reaction of the lids was first noted, an inflamed area developed on the chin, which gradually progressed to a typical vaccinia reaction.

Examination of the lids of both eyes showed pronounced redness, swelling and induration, with several ulcerations along the margins. There was moderate mucopurulent discharge. The conjunctiva of the right eye was mildly injected; that of the left eye was chemotic as well. The cornea did not stain with fluorescein. There was nontender swelling from eye to ear bilaterally.

A tentative diagnosis of vaccinia reaction was made. Subsequent stained smears and cultures of the discharge were negative for any causative organisms, and with the presence of the typical reaction of vaccinia on the arm and chin, the diagnosis was felt to be justified.

The temperature at the time of admission was 101 F. Sulfadiazine was administered orally, and within eight hours the temperature was essentially normal and remained so throughout the stay in the hospital, although administration of the sulfadiazine was discontinued in twelve hours.

Irrigations of boric acid were made every hour during the day, together with application of hot compresses for twenty minutes three times a day. Under this treatment there was decided improvement over the course of five days. At the time of discharge there was no edema of the lids of the right eye, no conjunctival injection and no corneal involvement, although there were three areas of excoriation with crust formation on the lower lid. The left eye showed mild edema of the lower lid and excoriation of the margin of the lid, with crust formation across its entire extent. The patient was discharged, with instructions to use hot compresses three times a day, followed by instillation of aqueous solution of metaphen (1:2,500).

COMMENT

Sulfadiazine was used for a short time in this case, since the diagnosis was at first questionable. Its use was discontinued after examination of smears revealed no causative organisms, and its effect was probably only to reduce the febrile reaction. In this respect, Atkinson and Scullard[1] reported that azosulfamide, sulfanilamide and sulfapyridine do not prevent the usual vaccinia reaction in rabbits.

As stated by Laval,[2] the sooner the secondary inoculation follows the primary one, the more severe and the more prolonged is the secondary reaction. In the case just reported this fact is well illustrated, since the secondary reaction

1. Atkinson, W. S., and Scullard, G.: Vaccinia with Ocular Involvement, Arch. Ophth. **23**:584 (March) 1940.

2. Laval, J.: Vaccinia of the Eyes, Arch. Ophth. **24**:367 (Aug.) 1940.

began only three days after vaccination, and there was a fairly severe constitutional response, as well as a rather marked reaction of the lids and conjunctiva.

It is important that inoculation of the cornea be prevented if possible, and measures should be taken to prevent the patient from rubbing or scratching the eyes.

Lesions of the lids and conjunctiva have been found to run a self-limited course, healing in seven to ten days, with no sequelae. Corneal involvement, however, requires a much longer period for healing, and visual impairment often results.

SUMMARY

In the case of autoinoculation of the eyelids following vaccination for smallpox here reported, the lesions healed without complications within the usual self-limited period.

It is of the utmost importance to prevent corneal involvement.

University Hospital.

Ophthalmologic Reviews

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OCULAR TUBERCULOSIS

ITS RELATION TO GENERAL TUBERCULOSIS

BENJAMIN L. GORDON, M.D.
ATLANTIC CITY, N. J.

There can no longer be any question that tuberculosis has prevailed from earliest times. The Old Testament perhaps refers to it when it alludes in three places to consumptive diseases (*shapahath*).[1] Among the symptoms are mentioned extreme wasting of the body and phthisis bulbi. In "Zechariah" the disease is described as follows: "In this shall be the plague . . . the flesh shall consume away, and the eyes shall consume away in their holes." In order to gain a clear knowledge of the history of tuberculosis of the eye, it is pertinent to present a brief historical sketch of general tuberculosis.

GENERAL REVIEW

As far back as the days of Hippocrates tuberculosis was recognized as a disease characterized by the breaking down and destruction of tissues. The name "phthisis," from the Greek word φθισις, meaning "wasting away," or "decay," was applied to this malady by Hippocrates. The father of medicine considered patients afflicted with this disease as incurable: "Many, and in fact, most of them died; and of those confined to bed I do not know of a single individual who survived for any considerable time."[1a] His description of the so-called facies hippocratica gives a typical picture of the last stage of consumption: "Hollow eyes, sharp nose, sunken temples, tense skin, cold ears, parched and discolored face, livid eyelids, open mouth and blanched lips."[1a]

Hippocrates had no other diagnostic procedures at his disposal than simple inspection and palpation. He had no stethoscope and no experience in percussion and auscultation. He had no tuberculin, no microscope and no roentgen rays to confirm his diagnosis. In spite of all these handicaps, his diagnoses appear to have been correct, and his therapeutics was far in advance of his time. He advised a young patient suffering from consumption to leave the city and rest in the sunshine, to eat nutritious foods and to imbibe much milk until his flesh rounded his frail frame and until his cough was gone and strength had returned. He stated the belief that phthisis was caused by small foci of pus.

Of the later ancient medical writers, none surpasses Aretaeus (about 50 A. D.) in his vivid description of tuberculosis. In his book *"De causis et signis morborum"* (The Causes and Diagnosis of Disease), he described with extraordinary accuracy:[2]

> . . . the curved nails, shrunken fingers, slender, sharpened nostrils, hollow, glazy eyes, cadaverous look and hue, the waste of muscles and startling prominence of bones, the scapulae standing off like the wings of a bird; the thin, veneer-like frames, the limbs, like pinions, the prominent throats and shallow chests.

He remarked that "moist and cold climates are the haunts of it."

Incidentally, Aretaeus was the first to make the following striking observation:[2]

> . . . Hemorrhage from the lungs is particularly dangerous, although patients do not despair even when near their end. The insensibility of the lungs to pain appears to me to be the cause of this, for pain is more dreadful than precarious; whereas in the absence of it, even serious illness is unaccompanied by fear of death and is more dangerous than dreadful.

The external signs of habitus phthisicus, which were described in great detail by ancient medical writers, have not changed up to the present time. Indeed, that frail, undersized, emaciated body, with the long, narrow, flat chest, in which the ribs stand out prominently, the chest bone is depressed and the shoulder blades project in the back like two wings, is the classic description

Read at a meeting of the Medical Staff of the Atlantic County Hospital for Tuberculous Diseases, Northfield, N. J., May 18, 1942.

1. Leviticus 26:16. Deuteronomy 28:22. Zechariah 14:12.

1a. Robinson, V.: The Story of Mankind, ed. 5, New York, Tudor Publishing Company, 1936, p. 510.

2. Aretaeus, cited by McLintock, J., and Strong, J.: Biblical Theological and Ecclesiastical Cyclopedia, New York, Harper and Brothers, 1894, vol. 6, p. 32.

still applicable to a large number of patients with tuberculosis.

There is no evidence that Hippocrates suspected contagion or infection to be the cause of these symptoms, although his contemporary, the historian Thucydides, in his "History of the Peloponnesian War," expressed a definite belief in the infectious character of plague and its transmission from one person to another. Describing the plague of Athens, he stated: "Nay, they [physicians] themselves died most of all, inasmuch as they most visited the sick."

Galen[3] indicated the infectious character of consumption when he stated that it is a matter of experience that persons who sleep in the same bed with tuberculous patients, as well as those who live long with them or wear their clothes and use their linens, contract tuberculosis.

In the hippocratic works, coxitis (tuberculous hip joint disease) is referred to, and its symptoms are correctly described: local and reflex pain coming on spontaneously, especially on movement of the limb; stiffness of the hip joint and the vertebral bones; lordosis (anterior convexity of the spine); bone necrosis; abscess formation, and spontaneous dislocation of the joint. The prognosis of coxitis, according to hippocratic writers, is poor as far as the use of the limbs is concerned. When ankylosis takes place, the limb becomes paralyzed. The hippocratic treatment consists of regulation of diet, internal administration of iron preparations and bleeding.[4]

Tuberculous bone disease was the scourge of the ages, even before pulmonary tuberculosis was recognized. Spondylitis, or tuberculosis of the spine, first described by Pott[5] (1713-1788) prevailed among ancients five millenniums ago.

While excavating in Grenelle, France, Palès[6] found two neolithic skeletons, one showing evidence of tuberculosis of the hip and the other signs of tuberculosis of the spine. Hofschlager[7] cited Bartel's statement to the effect that a neolithic skeleton from Heidelberg exhibited Pott's disease with kyphosis. Smith and Ruffer[8] recorded a case of Pott's disease in an Egyptian priest of Ammon of the twenty-first dynasty (about 1000 B. C.). In 1 case, Ruffer,[9] in a histologic study, noted an abscess of the right psoas muscle. Derry, according to Smith and Jones,[10] reported the discovery of several tuberculous spines at Thebes, dating from the twenty-third dynasty. Palès[6] mentioned the case of a child with coxalgia from the fifth dynasty and the case of an infant with a tuberculous hip, of 1900 B. C.

In America, Moodie[11] found Pott's disease in a Peruvian skeleton dating from prehistoric times. He expressed the opinion that the Peruvian Indians were widely afflicted with tuberculosis.

While Pott's disease is at present known to be caused by tuberculous infection of the spinal vertebrae, Percivall Pott, who first described the pathologic condition, attributed it to "scrofulous diathesis," which attacks children between the ages of 3 and 10 years. Many pathologic conditions known at present to be caused by the tubercle bacillus were attributed to various causes and were designated as different diseases. Thus, the term "scrofula" was applied to a number of pathologic conditions affecting the lymph glands of the neck, to various inflammatory diseases of the eyes and to chronic infections of the nose and throat. Tuberculosis of the lungs was designated by the name "consumption," "phthisis" or "white plague." Tuberculosis of the intestinal canal was known as "tabes mesenterica"; tuberculosis of the skin and eyelids, as "lupus"; tuberculosis of the conjunctiva, as "phlyctenules," or "phlyctenular conjunctivitis"; tuberculosis of the cornea, as "phlyctenular keratitis"; tuberculosis of the spine, as "Pott's disease," and tuberculosis of the bones and lymph glands, as "struma," "scrofula" or "king's evil."

While persons with phthisis were readily recognized as early as the days of Hippocrates, the world had to wait until the close of the seventeenth century for Franciscus de le boe Sylvius (1614-1672) to recognize the "little lumps" present in the tissue of consumptive

3. Galen believed in aerotherapy for tuberculosis. He ordered his patients to warm climates and to the sunny slopes of Vesuvius.

4. Lurje, S.: Studien über Chirurgie der Hippokratiker, Dorpat, C. Mattiesen, 1890, p. 117.

5. Pott recognized the cause of the disease, at least to the extent of calling it scrofula. His first paper on the subject bears the long title "Remarks on That Kind of Palsy of the Lower Limbs, Which Is Frequently Found to Accompany a Curvature of the Spine" (London, J. Johnson, 1779).

6. Palès, L.: Palèopathologie et pathologie comparative, Paris, Masson & Cie, 1930.

7. Hofschlager, R.: Von den Krankheiten des Vorgeschichtlichen Menschen, cited by Krogman, W. M.: The Pathology of Pre-and Proto-Historic Man, Ciba Symposia, May 1940. (Ciba)

8. Smith, G. E., and Ruffer, M. A.: Pott'sche Krankheit an einer ägyptischen Mumie aus der Zeit der 21 Dynastie (um 1000 v. Chr.), in Sudhoff, K. F., and Sticker, G.: Zur historischen Biologie der Krankheitserreger, Giessen, A. Töpelmann, 1910, no. 3, pp. 9-16.

9. Ruffer, M. A.: Studies in Paleopathology of Egypt, edited by R. L. Moodie, Chicago, University of Chicago Press, 1921.

10. Smith, G. E., and Jones, F. W.: The Archeological Survey of Nubia: Report for 1907-1908, Cairo, National Printing Department, 1910, vol. 2.

11. Moodie, R. L.: Paleopathology, Urbana, Ill., University of Illinois Press, 1923.

patients and to present an accurate description of their pathologic character. In the performance of a number of autopsies, Sylvius was impressed by the frequent occurrence of small, rounded, whitish gray bodies in the lungs of patients who in life had a condition diagnosed as phthisis. Sylvius came to the decision that these round bodies were the cause of phthisis. His conclusion was particularly prompted by the fact that pus commonly accompanies phthisical sputum; he compared these nodules with the commonly observed pus-producing inflammatory elevations, or papules, on the surface of the body. His explanation as to how and why they arose in the lungs and how they caused phthisis, however, is not conclusive, for his etiologic factors did not include the tubercle bacillus.

In the middle of the seventeenth century, the problem of tuberculosis attracted the serious attention of such celebrities as Thomas Sydenham (1624-1689), Thomas Willis (1621-1675) and Richard Morton, of England. Morton, in 1689, stated the opinion that the small bodies noted in the tissue started the ulcerative process in the lung. He also stated that one could die of the disease without showing any evidence of the small bodies, as they might be invisible. This last assertion anticipated the German maxim of later years, "Jedermann hat ein bischen Tuberculose am Ende." Other famous physicians interested in the subject were Gerard van Swieten, Boerhaave and Paul Barbette, of Netherlands; Jacob Manget, of Geneva, Switzerland; Sauvages, of France, and the famous anatomist, Giovanni Battista Morgagni, of Italy. The last investigator, while doing many autopsies in his anatomic studies, admitted that he had performed few on persons who had died of phthisis, adding that his master, Valsalva, had done practically none. It was not shortage of material that prevented autopsies on tuberculous cadavers. Morgagni readily admitted his great fear of contracting the disease from cadavers. He advised his young students also to shun them.

The association of these "little lumps" with consumption was proved by William Stark, a pupil of John Hunter, who, in 1785, while describing what is now known as miliary tuberculosis, pointed to these lesions as the cause of the disease, thus anticipating much that Laënnec was later to discover concerning tuberculosis. But Stark's work fell on deaf ears. The connection of these "little lumps" with consumption became a subject of controversy among students of pathology of various countries, among whom may be mentioned Cullen and Baillie, of England, and Portal, Kortum, Corvisart and Bichat, of France.

Bichat (1771-1802) died of tuberculosis, at the age of 31 years. One of his last utterances was: "Not much is really known about the pathology of phthisis, for few autopsies have been done because of the foolish fear among physicians that the disease is catching." His early death proved that phthisis was contagious. This brilliant scientist has been called the Napoleon of medicine. When his teacher, Corvisart (1755-1821), wrote to Napoleon: "Bichat has just fallen on a battlefield which numbers more than one victim; no one had done so much and so well in so short a time," the Corsican ordered the bust of Bichat placed in the Hotel Dieu.

The first to call attention to phthisis of the eye was Antoine Maitre-Jan[12] (born 1650), a

Fig. 1.—Marie François Xavier Bichat (1771-1802). From an engraving by H. Cook in Pettigrew's Medical Portrait Gallery, in the collection of the New York Academy of Medicine.

celebrated French physician of the seventeenth century. In 1707 he described the case of a soldier in whose eye an excrescence of the iris had sloughed through the cornea, and he attributed the condition to phthisis of the eye. He did not make clear on what grounds he based his conclusion. A century passed before the relation of ocular disease to phthisis of other organs of the body was pointed out again, this time by Autenrieth,[13] who described a choroidal tumor in a man who died later of generalized tuberculosis.

12. Antoine Maitre-Jan, sometimes known as the father of French medicine, author of "Traité des maladies de l'oeil, et des remèdes propres pour leur guérison," Troyes, J. le Febure, 1707 (p. 456); ed. 2, Paris, L. d'Houry, 1722; Paris, Breton, 1740.

13. Autenrieth, J. F. H.: Versuche für die praktische Heilkunde, Tübingen, J. G. Cotta, 1807, vol. 1, p. 309.

About the same time Gaspard Laurent Bayle (1774-1816), in his "Recherches sur la phthisis pulmonaire" (1810), described the "millet seed" bodies which he observed in cases of phthisis, calling them "tubercles," and he ascribed the pathologic changes in the patient to the process of caseation and to softening of the tubercles

Fig 2.—René Théophil Laennec (1781-1826). From an unsigned lithograph in the collection of the New York Academy of Medicine.

which he saw in many organs. After long and arduous clinical studies and hundreds of postmortem examinations of persons who had died of tuberculosis, he came to the conclusion that phthisis is an infectious disease and that the infection is caused by the inhalation or swallowing of poisonous material given off by persons suffering from this disease. Bayle himself died of tuberculosis in 1816, at the age of 42.

His intimate friend and junior collaborator, René Théophile Laennec (1781-1826), continued the investigation where Bayle left off. In spite of violent opposition from high places in the medical world, he supported Bayle's views and corroborated them with new evidence. He, too, made hundreds of autopsies, in many of which he observed diseased areas containing the "little lumps." Both investigators established the relation of these tubercles in the lungs to pulmonary phthisis and gave to them the name of tubercles. Bayle and Laënnec were convinced that these tubercles can be seen not only in the lungs but in any part of the body: skin, intestine, bones, brain, eyes and mucous membranes.

Laënnec demonstrated that phthisis not only hampers the organ it affects but produces a poison which spreads and affects the whole body, thus producing the symptoms characteristic of the disease. With the use of a microscope, but without the knowledge of the cell as the unit of tissue (the cell doctrine was promulgated in 1836), Laënnec maintained that the several forms of the disease depend on the development of the millet seed bodies. His ideas were accepted almost everywhere. He graphically described the tubercle as a "body composed of a gray, gelatinous form of infiltration, sometimes involving a whole lobe of a lung." The basis of all modern knowledge of tuberculosis, save only the important fact that the tubercles are produced by the action of the tubercle bacillus, came from Laennec's researches.

About the same time, the famous Italian anatomist and ophthalmologist Scarpa[14] described the case of a patient with an ocular condition which did not respond to local treatment as that of scrofulous ophthalmia of systemic origin. That the term "scrofulous ophthalmia" was applied to ocular phthisis may be inferred from the statement of the English ophthalmologist Mackenzie,[15] who, in 1830, while describing a case of conjunctivitis (which was probably phlyctenular conjunctivitis), asserted that "other scrofulous symptoms may be detected in almost every stage of the disorder, including disease of the joints, and tabes mesenterica."[16] The term tuberculosis was first used in 1839, by Dr. J. L. Schoenlein, of Zurich, Switzerland.

In 1831 von Jaeger[17] reported a case of tuberculosis of the eye in which the disease spread from the ciliary body, perforated the globe and produced phthisis bulbi. The diagnosis of

Fig. 3—Antonio Scarpa (1752-1832).

14. Scarpa, A.: Treatise on the Principal Diseases of the Eyes, translated by J. Briggs, London, T. Cadell & W. Davies, 1818.

15. Mackenzie, W.: A Practical Treatise on Diseases of the Eye, London, Longman [and others], 1830, p. 387.

16. Tabes mesenterica has always been considered of tuberculous origin.

17. von Jaeger, cited (page 2318) by W. S. Duke-Elder, from whose monumental work "Text-Book of Ophthalmology" (St. Louis, C. V. Mosby Company, 1941, vol. 3) I have derived valuable information in preparing this paper.

tuberculosis was confirmed after the enucleation of the organ of vision.

Prior to the middle of the nineteenth century the nature of ocular disease could only be surmised from the external appearance of the eye. Such gross changes as inflammation of the ocular tissues, discoloration of the cornea and impaired vision all too frequently occur only when disease

Fig. 4.—William Mackenzie.

s far advanced. The diagnosis of internal disease of the eye was largely speculative, the true character of the malady becoming obvious only after enucleation or during postmortem examination of the body. The difficulty in arriving at a correct diagnosis of ocular disease came from the lack of any adequate mechanical devices with which to determine pathologic changes in a living eye and to identify the location of such changes before the disease was well advanced.

The invention of the ophthalmoscope in 1851, by Hermann Ludwig Ferdinand von Helmholtz (1821-1894), an instrument which disclosed the deep structures of the eye and made clear any deviations from the normal state, not only revolutionized the field of ophthalmology but opened a new portal to the clinician in general. Many diseases of systemic origin and doubtful character became accurately diagnosed entities with the invention of the ophthalmoscope.

It may not be out of place here to quote von Helmholtz' own story of how he came on the idea of the ophthalmoscope: [18]

While preparing for the lecture, I first hit on the possibility of the ophthalmoscope . . . the ophthalmoscope has become the most popular, perhaps, of my scientific achievements, but I have already told the ophthalmologists how luck played an incomparably greater part than merit in this matter. I had to explain to my students the theory of ocular luminosity, which stemmed from Brücke. Actually, Brücke had missed the discovery of the ophthalmoscope by a hair's breadth. He had only neglected to ask himself the question: To which optical image do the rays returning from the luminous eye belong? Had he raised this question, he could have answered it just as quickly as I did, and the ophthalmoscope would have been discovered. I was considering the problem from different angles, in order to see how I could present it most simply to my audience, and while so engaged I hit upon the aforementioned question. As a result of my medical studies, I was well acquainted with the difficulties confronting ophthalmologists in those conditions which at that time were lumped together under the term amaurosis. I immediately set about to construct the instrument out of spectacle lenses and cover glasses for microscopic preparations. At first it was still quite difficult to use, and without a firm theoretic conviction that it must work, I would perhaps not have persevered in my efforts. But after about eight days I had the great pleasure of being the first to see clearly a living human retina.

As has often been the case with medical innovations, his discovery did not receive undivided support from members of the medical profession. One distinguished ophthalmologic colleague told the discoverer that he should never use the instrument, for it would be too dangerous to admit naked light into the diseased eye! Another expressed the opinion that the mirror

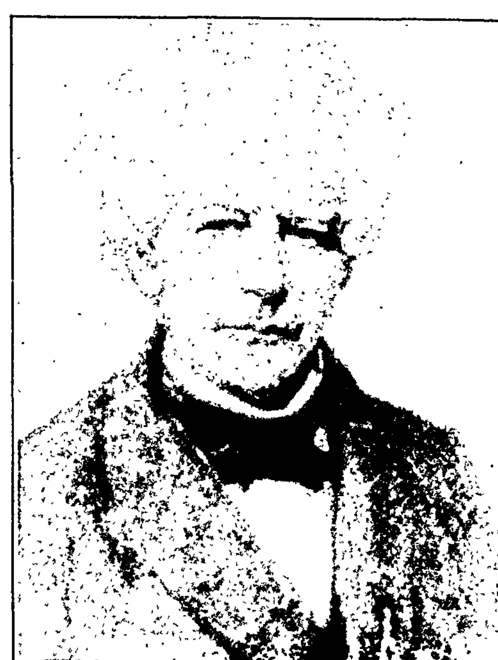

Fig. 5.—Fred von Jaeger (1784-1871).

might be of service to oculists with defective eyesight. For his part, he had good eyes and wanted none of it.

After the discovery of his Augenspiegel, not a year passed that von Helmholtz did not make some new discoveries. His investigations delved into the realms of physics, physiology, medicine, optics, chemistry, acoustics, electricity and

18. Von Helmholtz was preparing a lecture for his class at the University of Königsberg, where he occupied the chair of physiology, on the subject of ocular luminosity in certain animals, such as the rabbit and cat (Erinnerungen, in Vorträge und Reden, Braunschweig, F. Vieweg & Sohn, 1896, vol. 1). His modesty, refined life and simple taste he inherited from his mother, who was a Hanovarian lady, a lineal descendant of the great Quaker, William Penn.

mathematics. His work "Physiologic Optics" (1856-1860) is by far the most important book that has ever appeared on the physiology and physics of vision. By his invention of the ophthalmometer, he measured the radiuses of curvature of the crystalline lens for near and far vision. He investigated the mechanism of accommodation by which the eye can focus within certain limits and the movements of the eyeballs necessary to secure single vision with two eyes. He revived and gave new force to the theory of color vision associated with the name of Thomas Young, based on the three primary colors, and he applied the theory to the explanation of color blindness. The most important of his discoveries, however, was the ophthalmoscope. When von Graefe first saw the fundus of the living eye, he exclaimed, "Helmholtz has unfolded to us a new world."

Fig 6.—Albrecht von Graefe (1828-1870).

Four years after the invention of the ophthalmoscope, Albrecht von Graefe (1828-1870) and Friedrich Moritz H. Heymann (1828-1871) described renal retinitis, thus corroborating the diagnosis of the internist, or even calling his attention to the fact that the patient's ophthalmic condition was due to renal dysfunction. In 1853, two years after the invention of the ophthalmoscope, Coccius observed detachment of the retina, and in 1855 Liebreich noted thrombosis of the central vein. In 1860 von Graefe observed bilateral papilledema and embolism of the central artery. A new conception of glaucoma was made possible, and the cause of amaurosis in cases in which the external portion of the eye exhibited no pathologic signs—a problem throughout the ages—at last became known.[19]

19. Sorsby, A.: A Short History of Ophthalmology, London, John Bale, Sons & Danielsson, 1933, p. 81.

What the discovery of roentgen rays, fifty years later, has been to pulmonary tuberculosis, the invention of the ophthalmoscope was to ocular tuberculosis. Five years after von Helmholtz' invention, Jaeger observed tubercles in the choroid with the ophthalmoscope.[17] The tuberculous character of these lesions was corroborated microscopically by Manz[20] (1858), who first reported the case and recorded 2 additional ones in 1866. Cohnheim[21] (1867) demonstrated that the choroidal nodules seen in the eye clinically were pathologically identical with the tubercles seen elsewhere in the body. His investigations proved that they occur more frequently than had been supposed. Similar conclusions were reached by von Graefe and Leber, in Germany (1868), and by Wells, in England (1868).[22] In 1874 Köster[23] described tubercles of the conjunctiva. About the same time Horner[24] diagnosed with the ophthalmoscope for the first time conglobate tubercles of the choroid in man. Some time later Jessop[25] described a case of tuberculous conjunctivitis following injury.

The recognition of tuberculosis was greatly advanced by the investigations of Jean Antoine Villemin (1827-1892).[26] Villemin demonstrated the infectious nature of the tubercle by injecting tuberculous tissue into rabbits. He told his assistants in the army in which he was a surgeon that "the phthisical soldier is to his messmate what the glanderous horse is to his yoke fellow." Villemin was first to observe that the tubercles were caused by living entities. He was, however, unable to identify the etiologic factor with his microscope.

Soon after, von Baumgarten[27] inoculated the anterior chamber of rabbits with tuberculous tissue and, after removing the eyes for histologic study, observed that migratory cells gather

20. Manz, W.: Tuberculose der Chorioidea, Arch. f. Ophth **4** (pt. 2):120, 1858.

21. Cohnheim, J.: Ueber Tuberculose der Chorioidea, Arch. f. path. Anat. **34**:49, 1867.

22. von Graefe, A., and Leber, T.: Ueber Aderhaut-tuberkeln, Arch. f. Ophth. **14** (pt. 1):183, 1868.

23. Köster, cited by Harman,[31] p. 140.

24. Horner, cited by Haab, O.: Atlas and Epitome of *Ophthalmoscopy and Ophthalmoscopic Diagnosis*, edited by G. de Schweinitz, Philadelphia, W. B. Saunders Company, 1909, page opposite figure 76.

25. Jessop, W. H.: Tuberculosis of the Conjunctiva, Tr. Ophth. Soc. U. Kingdom **20**:51, 1900; in Carpenter, G, and Stephenson, S.: Tuberculosis of the Choroid, in Reports of the Society for the Study of Diseases of Children, London, J. & A. Churchill, 1900-1901, vol. 1, p. 169.

26. Villemin, cited by Piersol, G. M., and Bortz, E. L.: Cyclopedia of Medicine, Philadelphia, F. A. Davis Company, 1935, vol. 12, pp. 232-244.

27. von Baumgarten, P., cited by Flick, L. F.: Tuberculosis, Philadelphia, The Author, 1937, p. 69.

around the infected material, with tubercle bacilli crowded in the center.

Knowledge of the etiologic agent of tuberculosis, which Sylvius, Laënnec and Villemin attributed to the tubercles observed in the diseased tissues, reached its climax with the great discovery of Robert Koch (1843-1910), who in

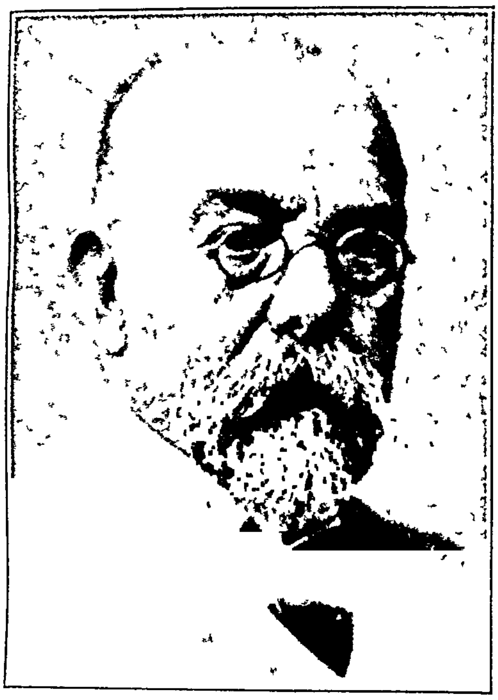

Fig. 7.—Robert Koch (1843-1910). From a photoengraving in the collection of the New York Academy of Medicine.

1882 stirred the scientific world by the announcement of his discovery of a living organism (the tubercle bacillus) in sections of the tubercles. He proved the accuracy of his observations by producing tuberculosis in guinea pigs inoculated with cultures of this bacillus. Koch, however, had a difficult task to convince his medical colleagues that he had made a momentous discovery, for he was unknown to the scientific world. He suddenly emerged from obscurity, to be ranked among the greatest scientists of his age.

A short biographic sketch of Koch may be apropos at this point. There was nothing eventful in his early life. His family was in modest circumstances. There was little reserve for luxuries or for giving the children a higher education. When young Robert was about to finish the local high school, his parents planned for him to learn the shoemaking trade. Just then an unforeseen improvement took place in the financial condition of the elder Koch, which enabled him to send his son to the University of Göttingen, where the celebrated pathologist (Frederick Gustave) Jacob Henle (1809-1885), the author of "A Handbook on Rational Pathology," was professor. At that period Henle published his famous essay, entitled "Miasmata and Contagia," which was widely discussed in scientific medical circles. It contained the first clear statement in modern terms that infectious diseases are due to specific organisms. It is likely that this famous teacher had a great influence over young Koch's future work.

After receiving his doctorate, Koch disappeared from academic circles for ten years. His meager financial status compelled him to earn a livelihood immediately. He started his medical career as an obscure country doctor in the little town of Wollstein, in the province of Pausen, Czechoslovakia. This town had a mixed population, made up largely of Czechs and Poles. There were certainly no laboratory facilities. All that he possessed was a microscope, which he had purchased while at the university. One can be certain that he used it at his office whenever he could spare time from his medical duties.

In those days bacteriology was a branch of botany, and the leading authority on that subject was Ferdinand Cohn, of Breslau. Any one who wanted information on the parasitism of the algae and fungi applied to Ferdinand Cohn. From a letter sent to Cohn by Koch in 1876, it is clear that the latter did not spend his ten years in Wollstein idly. The letter reads: "After many vain attempts, I have finally been successful in discovering the process of development of the anthrax bacillus. After many experiments, I believe that I am able to state the results of these researches with sufficient certainty. Before, however, I bring this into the open, I respectfully appeal to you, esteemed Herr Professor, as the foremost authority on bacteria, to give me your judgment regarding this discovery."

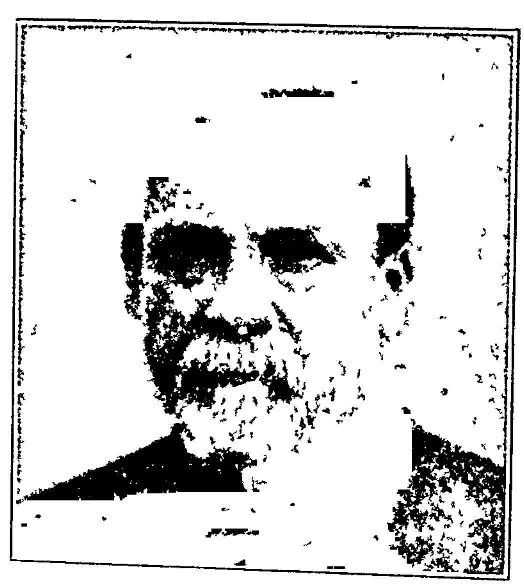

Fig. 8.—Louis Pasteur (1822-1895). From a photograph in the collection of the New York Academy of Medicine.

The epoch-making discoveries of Pasteur undoubtedly had a great influence on Koch's re-

search. One evening, he read in a scientific journal that this French chemist had demonstrated that microscopic plant germs could live and thrive in the bodies of men and animals and that the presence and growth of some of them were attended by disease. Soon afterward, Koch seriously began the task of developing new technical methods, which became the basis of modern bacteriologic technic. He separated and identified bacteria; he grew them in pure culture; he stained them and photographed them.

Koch and his colleagues demonstrated that the tubercles described seventy-eight years before by Laënnec, and fifteen years before by Villemin, were caused by the action of bacteria on the tissues, and that the dissemination of the disease was produced by the spread of these tubercle-forming bacilli.[28]

It was on the evening of March 24, 1882 that Koch startled the Physiological Society of Berlin by announcing his discovery of the tubercle bacillus. He was not satisfied with merely discovering the cause of tuberculosis. He tried to find means of preventing and curing this disease. In 1890 he prematurely announced that he had discovered a remedy for tuberculosis, which revelation was received with great enthusiasm everywhere. As a therapeutist, however, he failed to fulfil the expectation and hope which his announcement raised among millions of people. Although his tuberculin as a therapy for tuberculosis was a failure, the discovery proved to be of diagnostic value. It furnishes a test for the detection of the presence of either active or arrested tuberculosis in the body, although it does not differentiate between the two grades of the disease and does not show the place where the pathologic condition is located. Five years after Koch's discovery (1887), Becker,[29] of Heidelberg, observed a growth in the choroid, just behind the ciliary region, of typical tuberculous structure containing bacilli. He noted smaller tubercles in other parts of the choroid.

The last link in the chain surrounding the diagnosis of tuberculosis came with the discovery of roentgen rays, in 1895, by Wilhelm Conrad Roentgen, professor of physics at the University of Strasbourg, who, while experimenting with electric discharges passing through vacuum tubes, discovered this peculiar kind of energy. This disclosure came to him unexpectedly. One day, while examining a vacuum tube in a black box, he noticed that a paper screen, covered with barium platinocyanide, which accidentally stood nearby, became fluorescent. His curiosity became aroused at this strange spectacle. He soon discovered that the unknown radiations from the tube could pass through substances ordinarily opaque to light and that these radiations possessed the power of affecting photographic plates. Two months later he announced his discovery, which he named x-rays.

Roentgen rays are of only indirect value in the diagnosis of ocular tuberculosis, however; their importance lies in their identifying and localizing tuberculous conditions in other tissues of the body.

RELATION OF OCULAR TUBERCULOSIS TO TUBERCULOSIS IN OTHER ORGANS OF THE BODY

While, as has been shown, the eye, like other organs of the body, may be attacked by the tubercle bacillus, the method of attack has not yet been definitely established. That ocular tissue reacts to micro-organisms and toxins originating from a remote part of the body cannot be disputed. Cases of metastatic ophthalmitis are known to have resulted from pyogenic bacteria carried to the eye by the blood and lymph centers from infected areas of near and distant organs. Iridocyclitis has often been traced to gonorrheal prostatitis, and the gonorrheal chacacter of the infection was demonstrated by many observers. Deutschmann demonstrated gonococci in the mucous discharge of the conjunctiva, which he thought entered the eye by metastasis. A similar observation was made by Parinaud and Duane.[29a] Morax stated that scattered gonococci may be seen in cases of gonococcic conjunctivitis, and that one must not conclude from a negative examination for gonococci that the inflammation is due to pure toxin. The organisms themselves, although not found, cannot be excluded. McKee[29b] reported a case of metastatic gonorrheal conjunctivitis in which the gonococcus was demonstrated.

I have recently observed a similar case in a young man, in Atlantic City, N. J. On the other

28. Koch laid down three cardinal rules with reference to bacteria: 1. A specific organism must be present in all cases of the disease. 2. It must be cultivated in pure culture. 3. It must produce the same disease when injected in healthy animals.

29. Becker, cited by Neese, E.: A Contribution to Tuberculosis of the Eye, Arch. Ophth. **16**:434, 1887.

29a. Fuchs, E.: Textbook of Ophthalmology, authorized translation from the eleventh and greatly enlarged edition of the German by Alexander Duane, ed. 3, Philadelphia, J. B. Lippincott Company, 1908.

29b. McKee, S H.: Demonstration of the Gonococcus in Smear and Culture, Ophthalmology **7**:462 (July) 1909.

hand, Arnold Knapp, in a number of cases under his observation, could not find gonococci in the conjunctiva, and cultures were sterile. Spirochetes have been observed in the eyes of persons affected with syphilis in other parts of the body; but the tuberculous origin of many obscure ocular diseases attributed to the tubercle bacillus has never been adequately demonstrated.

Those who have the opportunity of observing tuberculous patients in institutions have been surprised at the infrequency of ocular disease among inmates. The eye appears to possess a peculiar immunity to tuberculous infection among patients with pulmonary and other forms of tuberculosis. Both the intrinsic spread of the bacilli and the extrinsic dissemination via the sputum appear to have a negligible effect on the visual organs. Treponema pallidum in its active state readily attacks the uvea and the optic nerve irrespective of the location of the initial lesion, and the gonococcus of Neisser, which usually lodges in the genital organs, frequently involves the conjunctiva; but the bacillus of tuberculosis in the lungs or other tissues of the body seldom affects the eye. In the institutions for the blind may be seen many children who were blinded in consequence of acquired or inherited syphilitic infection or as a result of ophthalmia neonatorum. But cases of blindness due to the tubercle bacillus are rarely seen in such institutions.

Von Michel was the first in Germany to demonstrate the presence of tubercle bacilli in the eye. Since his time many workers, by injecting living or dead tubercle bacilli into the carotid artery of rabbits, have succeeded in producing acute and chronic forms of iritis, tubercles in the iris, nodules on the pupillary margins and circumscribed infiltrates in the cornea. The condition produced by this method showed a striking resemblance to certain chronic forms of clinical iritis, an observation in support of the conclusion that the latter is often tuberculous. (Von Michel, however, did not accept the importance of tuberculin therapy, as suggested by von Hippel.)

Denig,[30] who was an assistant to von Michel in 1895, observing this strange phenomenon of the tubercle bacilli on the human eye, was prompted to declare that tuberculosis of the eye is seldom observed among persons with active tuberculosis of the lungs. In an analysis of 65 cases of pulmonary tuberculosis, 90 cases of tuberculosis in the joints and bones and 20 cases of tuberculosis of the lymph glands, a total of 175 cases of active tuberculosis, Denig found only 5 cases of ocular metastasis, while of 86 cases in which the anterior uveal tract was affected, no evidence of systemic disease was apparent in 76.

In England, Harman[31] (1908) asserted:

> The infection of the eye and of its accessory structures by the tubercle bacillus is one of the rarer forms of disease of which the eye is liable. If we compare the frequency of the effects of this infection with that of another organism—the spirochaeta pallida—which also produces granulomatous inflammations, there can be no hesitation in asserting that tuberculous diseases of the eye are rare.

Whitehead, another English ophthalmologist, in postmortem examinations of patients with ocular tuberculosis who subsequently died of fatal injuries in World War I, noted that 42 per cent exhibited no pathologic lesion elsewhere in the body. The same report came from Egypt. Wilson[32] stated that within seventeen years 21 cases of ocular tuberculosis were recorded by the pathologists of the Government Ophthalmic Hospital. In none of these cases did the surgeons notice any signs of tuberculosis in other parts of the body.

In an analysis of 72 cases of uveal disease in adults, Rohrschneider and Reiners[33] observed minor, dormant and closed remnants of tuberculous processes in 64 cases. In 6 other cases formerly active pulmonary tuberculous foci were inactive at the time of examination. In only 2 cases was active tuberculosis present. These authors found no difference betweeen the cases associated with positive clinical signs of pulmonary tuberculosis and those with less suspicious evidence. They consequently asserted that a diagnosis based on the presence of tuberculous foci in cases of ocular disease is not conclusive. They cited Marchesani,[34] who expressed the opinion that the tuberculous origin of chronic uveitis is not as well established as has been assumed by many authors. Marchesani particularly questioned the tuberculous origin of recurring vitreous hemorrhages in adolescence and suggested that the possibility of Buerger's disease should be considered.

30. Denig, R.: Ueber der Häufigkeit der Localtuberkulose des Auges, Arch. f. Augenh. **31**:359, 1895.

31. Harman, N. B., in Kelynack, T. N.: Tuberculosis in Infancy and Children, New York, William Wood & Company, 1908, pp. 130-132.

32. Wilson, R. P.: Tuberculosis of the Eyeball and Adnexa in Egypt, Mem. Ophthalmic Lab., Giza, Ann. Rep., 1929, p. 46.

33. Rohrschneider, W., and Reiners, H.: Die Bewertung des Lungenbefundes bei tuberkuloseverdächtigen Augenkrankheiten, Klin. Monatsbl. f. Augenh. **96**:778, 1936.

34. Marchesani, O.: In welchem Umfange darf bei Erkrankungen des Auges tuberkulöse Aetiologie heute als sichergestellt gelten? Klin. Wchnschr. **11**:1921, 1932.

In the United States, Goldenburg and Fabricant,[35] in a paper read before the section of ophthalmology of the Americal Medical Association based on the observation of 1,073 sanatorium patients with proved tuberculosis, reported that 7 patients had pathologic changes in the iris, a percentage of 0.67, of which the lesions of only 3, or 0.27 per cent, could seriously be considered tuberculous. Examination of the fundus of 914 patients revealed deviation from the normal in 78, in only 19 of whom, or 2.08 per cent, the condition could possibly be considered tuberculous. Of these 19 patients, 18 had unilateral involvement, an occurrence which would exclude the infection by toxin.

In a paper read before the section of ophthalmology of the New York Academy of Medicine, Eggston,[36] came to the following conclusion:

> The ocular lesions frequently diagnosed as tuberculosis in a patient with positive reactions to tuberculin are really not due to infection by tuberculous bacteria, with the formation of a tubercle, but are of an allergic nature, if they are in any way related to tuberculosis. Actual tuberculous infection of the eye is relatively rare.
>
> Injections of tuberculin are of value in the allergic cases if given properly in order to desensitize the patient, but of questionable value in the active tuberculous ones.

Five years of experience with tuberculous patients in the Atlantic County Hospital for tuberculosis has led me to similar conclusions. I have encountered no anomalies of the eye which I could definitely ascribe to pulmonary infection. The most common complaints were fatigue, tenderness, burning sensations in the eyes and, frequently, supraorbital pain, symptoms generally due to refractive errors and muscular asthenopia, which are more common among patients who are confined to bed and read a good deal under unfavorable conditions. Another patient, with a history of head injury, sustained several years previously, had diplopia. A patient with plastic iritis of questionable origin also exhibited a positive Wassermann reaction. Another patient had atrophy of one nerve head, the cause of which was not clear. Peter[36a] found no uveal lesions in 300 cases of the last stages of pulmonary tuberculosis.

Woods[37] stated that the diagnosis of ocular tuberculosis must be based on the course and character of the lesion, on the exclusion of other etiologic factors and on a study of the general tuberculous status of the patient. Reactions to tuberculin are of value only when strongly positive. Weakly positive or negative reactions are of no significance for or against the diagnosis of ocular tuberculosis. Even when nodules are noted in the iris or choroid, some authors question their tuberculous origin. Kapuscinski[38] of Posen, Poland, reported a case of iridocyclitis with "tuberculous" nodules on the iris of each eye. However, all the clinical tests for tuberculosis, including injections of tuberculin in doses up to 25 mg., as well as inoculation of material from the nodule in a guinea pig and a rabbit, gave completely negative reactions. After reviewing the literature on the subject, the author concluded that the problem of ocular tuberculosis deserves a more critical consideration than has generally been given it.

On the other hand, 365 patients with ocular tuberculosis were reported by Mehlmack[39] from Hertel's clinic, in Leipzig. The largest number of patients were between 20 and 50 years of age. The majority of the patients—between the twentieth and the thirtieth year of life—were women. The uveal tract was the seat of the disease in 80 per cent of patients. In practically all the patients with uveal tuberculosis primary lesions were observed in the chest. The tuberculin reaction was positive in practically all the patients in whom clinical and roentgenographic examination revealed inactive tuberculosis, but in a number of the very young patients and in some of the women during the menopause the reaction was negative in spite of definite evidence of active generalized tuberculosis, such as involvement of the lymph glands, with or without pulmonary involvement. Stock[39a] contended that chronic inflammations of the eye and its adnexa, particularly chronic uveitis, are tuberculous in origin. Lagrange[39b] expressed a similar opinion.

Werdenberg[40] observed a notable parallelism between tuberculous lesions of the eye and those of the thorax:

> Ocular tuberculosis . . . is expressed by the presence of an ascending infection from the tuberculous hilar

35. Goldenburg, M., and Fabricant, N. D.: The Eye in the Tuberculous Patient, Arch. Ophth. **5**:66 (Jan.) 1931.

36. Eggston, A. A.: The Use of Tuberculin in Diagnosis and Treatment in Ophthalmology, Arch. Ophth. **8**:671 (Nov.) 1932.

36a. Peter, L. C.: Eye Phenomena Observed in 300 Cases of Pulmonary Tuberculosis, Am. J. Ophth. **33**: 105, 1916.

37. Woods, A. C.: Problem of Ocular Tuberculosis, Am. J. Ophth. **21**:366, 1938.

38. Kapuscinski, W.: Ocular Tuberculosis, Arch. Ophth. **22**:934 (Nov.) 1939.

39. Mehlmack, F.: Zur Klinik der Augentuberkulose, Arch. f. Augenh. **110**:39, 1936.

39a. Stock, W.: Tuberkulose als Aetiologie der chronischen Entzündungen des Auges und seiner Adnexe besonders der chronischen Uveitis, Arch. f. Ophth. **66**: 1, 1907.

39b. Lagrange, H.: La tuberculose du tractus uvéal, Paris, G. Doin, 1923.

40. Werdenberg, E.: Typischer und atypischer Krankheitsverlauf bei Augentuberkulose, Klin. Monatsbl. f. Augenh. **85**:98, 1930.

glands.' . . . One must bear in mind that mild and severe forms of this mediastinal disease may give rise to equally malignant tuberculous lesions in the eyes. Often the roentgenogram fails to reveal the source of the disease; nevertheless, in the presence of a malignant intraocular process, one must infer that a similarly malignant tuberculous condition is active elsewhere in the body. Finnoff,[40a] in his studies of ocular tuberculosis, concluded that chronic uveitis is frequently tuberculous. The tubercle bacilli enter the eye from known or unknown foci through the blood. In most cases tuberculous uveitis is characterized by nodules. No part of the uvea is invulnerable. Obscure chronic inflammation is often due to tubercle bacilli, except for that of the conjunctiva and cornea. In most cases the foci are relatively inactive and are often impossible to locate with present methods of examination.

Urbanek[41] came to similar conclusions. In a large number of cases of ocular disease diagnosed as tuberculous uveitis and other inflammatory conditions, roentgenographic examination revealed that the lungs were not normal. Tuberculosis in the lungs most frequently associated with ocular disease is of the mildest type and presents few symptoms or physical signs. The tubercle bacilli in cases of this type seem to lack the ability to produce the typical granulation tissue with central caseation, or even characteristic giant cells. Urbanek claimed that he noted the tubercle bacilli in the blood stream of patients suffering from episcleritis and sclerosing keratitis. He expressed the opinion that the hypodermic injection of preparations of tuberculin is the best method of diagnosis. The allergic reaction of the patient to the tuberculin antigen must be carefully noted. Administration of the test to about 100 adults with scrofulous keratoconjunctivitis proved that the majority reacted positively. Arnold Knapp, in 1 case, obtained by culture a tubercle bacillus from the aqueous in a case of iridocyclitis with sclerosing keratitis.

Krasso[42] stated:

It is common knowledge that a disease of the eye may be of tuberculous origin even though the histologic examination shows no typical tuberculoma. With definite evidence of a tuberculous origin the involvement in question may display a nonspecific simple inflammatory reaction. In the etiologic diagnosis of tuberculosis of the eye one should make a diagnosis . . . in addition to bacillary and histologic investigations.

Lloyd[43] went so far as to say that most of the so-called focal infections of the eye are really tuberculous. Relapses, he stated, are due to periods of lowered resistance. He stated the opinion that intraocular hemorrhage in young persons is of tuberculous origin unless proved otherwise.

Other observers even offered the opinion that a tuberculous origin may be assigned to all obscure ocular conditions. Pillat,[44] for example, observed that the list of ocular diseases which are considered tuberculous in the absence of a positive reaction to tuberculin may be extended. The ophthalmologist cannot reject a tuberculous cause because of a negative Pirquet or Mantoux reaction. One must remember that there are tuberculous diseases in which the Mantoux reaction is negative but the reaction to Moro's tuberculin in an ointment base is positive, and, further, that the Mantoux reaction, although negative for forty-eight hours, may become positive in eight days.

A school headed by Löwenstein[45] and Meller,[46] of Vienna, maintained that tuberculosis not only is the cause of ocular disease in which tubercles can be demonstrated but may be the etiologic factor in a host of ocular inflammatory processes of doubtful character, especially those of a recurrent or chronic type, even though a tuberculous origin cannot be demonstrated elsewhere. Fontana[47] asserted that "focal infection," a favorite etiologic factor with oculists a generation ago, was in reality tuberculous in nature.

Fontana's allusion to focal infection brings to mind a similar controversy with reference to the cause of obscure chronic ocular diseases. After Lang[48] (1913) made known his observations on the influence of dental sepsis on diseases of the eye, the effect of infected teeth on the eye was seriously discussed by members of the medical profession. It was shown that, aside from the structural proximity to and the anatomic relation of the visual organ to the teeth, there was a special selectivity of the

40a. Finnoff, W. C.: Ocular Tuberculosis, Arch. Ophth. **53**:130, 1924; Tuberculosis in the Etiology of Acute Iritis, Am. J. Ophth. **14**:127, 1931; Relation of Tuberculosis to Chronic Uveitis, ibid. **14**:1208, 1931.

41. Urbanek, J.: Ocular Tuberculosis, Tr. Ophth. Soc. U. Kingdom **52**:227, 1932. Urbanek, J., and Meller: Tubercle Bacilli in Blood in Diseases of the Eye, Arch. Ophth. **4**:262 (Aug.) 1930.

42. Krassó, J.: Diagnosis of Tuberculous Diseases of the Eye and Their Treatment with Subconjunctival Injections of Virulent Human Tubercle Bacilli, Orvosképzés **25**:267, 1935; abstracted, Arch. Ophth. **17**:1145 (June) 1937.

43. Lloyd, R. I.: Tuberculosis of the Eye, Am. J. Ophth. **13**:753, 1930.

44. Pillat, A., in discussion on papers by Krückmann, Rohrschneider and Volkel, Arch. Ophth. **23**:420 (Feb.) 1940.

45. Löwenstein, E.: Das Vorkommen der Tuberkelbazillämie bei verscheidenen Krankheiten, München. med. Wchnschr. **78**:261, 1931.

46. Meller, J.: Tub. bacil. in das Blut des kranke Auge, Ztschr. f. Augenh. **13**:41, 1930.

47. Fontana, G.: Ricerche citologiche sul sangue di individui affetti da congiuntivite flittenulare, Boll. d'ocul. **11**:582, 1932.

48. Lang, W.: The Influence of Chronic Sepsis upon Eye Diseases, Lancet **1**:1368, 1913.

micro-organisms and toxins of dental disease for ocular tissues. Rosenow,[49] of the Mayo Clinic, demonstrated that when bacteria are taken from diseased teeth and injected in the blood stream of animals, they produce diseases of the eye and that, within limitations, this selectivity is characteristic of the bacterial strain and is manifested through several cultural transplants of the organism. Zanettin[50] produced plastic iridocyclitis in animals by injecting a strain of the streptococcus from a suspected tooth of a person with iridocyclitis.

Older ophthalmologists well remember how frequently patients were deprived of their teeth on the mere supposition that the ocular lesion was caused by dental caries or pyorrhea. Lang's dictum that "it is better to lose thirty-two teeth than one eye" was taken as justification for wholesale extraction of teeth. All arguments that only a small proportion of patients with dental disease suffer from ocular complications, and that the larger number of patients with pyorrhea and alveolar abscesses applying for dental treatment have no ocular lesions were of no avail. The fact that the removal of a septic tooth does occasionally result in clearing up of a chronic inflammatory condition of the eye was sufficient to lead some workers to ascribe all such obscure chronic lesions to dental sepsis. No consideration was given to the fact that for each case of cure by dental extraction reported, many cases in which the treatment was unsuccessful have never been made public. The argument against dental sepsis as an etiologic factor in all ocular disease may be applied with more force to tuberculosis, even in cases in which tuberculous lesions have been detected elsewhere in the body.

While uveal tuberculosis is frequently difficult to diagnose, tuberculosis of the external segment of the eye in most instances may be ascertained by laboratory investigation. Eyre[51] studied 206 patients with tuberculous conjunctivitis, for all of whom the diagnosis was based on the presence of the bacillus in the conjunctival sac and on reproduction of the disease in animals by means of inoculation. In 46 patients he observed ulcerations of the conjunctiva; in 25, miliary tubercles; in 80, hypertrophic granulations; in 46, lupus, and in 9, pedunculated tumors. Of 2,500 patients with ophthalmic disease in London hospitals, he saw only 8 with tuberculous conjunctivitis. As to the method of invasion, he expressed the belief that the disease is secondary to nasolaryngeal tuberculosis. Frequently a slight trauma or breaking down of a phlyctenule furnishes a nidus for the growth of the bacilli.

Eyre did not agree with Arlt, who was first to express the opinion that tuberculous conjunctivitis is caused by the spread of the disease from the face. Arlt based his opinion on a case of tuberculous conjunctivitis encountered in 1864, in which the disease was produced by the spread of lupus. Lundsgaard[52] expressed the opinion that tuberculous conjunctivitis is an endogenous infection and differs from lupus, which is ectogenous. These two lesions, according to Lundsgaard, differ also with respect to the age incidence. Conjunctival tuberculosis affects persons under 20, while lupus occurs in adults up to 52 years of age. Tuberculous conjunctivitis, also, is always unilateral and is more severe than lupus, involving the upper lid and the periocular glands, and is often associated with swelling and abscess formation.

Tuberculous conjunctivitis is a disease characterized by the presence of one or more ulcers, which are covered with necrotic, dirty gray material, through which loops of granulation tissue protrude. The ulcers spread slowly, with little disposition to heal. The lesions appear usually in the tarsal conjunctiva. The lymph glands become swollen, the glandular involvement being followed by swelling of the glands of the lower jaw and the neck; the glands, however, are not the primary source of infection, as they may be with tuberculous uveitis. According to this description, tuberculous conjunctivitis is a primary disease of serious consequence.

In Egypt, according to Wilson,[32] the tubercle bacilli seem to have a special predilection for the conjunctival membrane; the incidence of tuberculous conjunctivitis is one-third that of all forms of tuberculosis. The disease plays a more important part in the causation of lesions of the cornea than is usually admitted. According to Wilson, tuberculous conjunctivitis is essentially a disease of early life. Histologically the ocular lesions do not differ from tuberculous

49. Rosenow, E. C.: Iritis and Other Ocular Lesions on Intravenous Injection of Streptococci, J. Infect. Dis. **17**:403, 1915.

50. Zanettin, G.: Infezioni focali e malattie oculari, Ann. di ottal. e clin. ocul. **62**:588, 695 and 786, 1934.

51. Eyre, cited by McKee, S. H., in Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, pp. 407-408.

52. Lundsgaard, K. K. K.: Tuberculosis Conjunctivae: Eventual Fate of the Patients, Acta ophth. **1**:39, 1923; cited by Blegvad, O.: Die Konjunktivaltuberkulose, ibid. **11**:345, 1933. J. M. Ball, many years ago, demonstrated that lupus attacks the conjunctiva, that over 50 per cent of cases of tuberculosis of the conjunctiva are due to lupus (Modern Ophthalmology, ed. 3, Philadelphia, F. A. Davis Company, 1913, p. 289).

foci seen in other parts of the body. In many cases granular conjunctivitis is in reality tuberculosis of the conjunctiva. Haab described a case of trachoma which on closer examination proved to be of tuberculous origin.

Benalioua [53] stated the opinion that primary tuberculous infection of the conjunctiva, long considered grave, has in reality a favorable prognosis, cures occurring without any complication except bacillary migrations, which are without danger, the bacilli no doubt being conveyed by an erythema. The disease is one of children and young adults and is seen more frequently in females than in males. It is unilateral and sluggish and is associated with various lesions of the mucous membrane, and frequently with numerous caseous glands. The author expressed the belief that the treatment should not be too aggressive and should be systemic. This favorable prognosis applies particularly to the phlyctenular form of conjunctivitis.

Phlyctenulosis, derived from the Greek word *φλυκταινα*, meaning a "blister," is really a misnomer, since the lesion from its very beginning, is not a blister, but a pustule, which quickly breaks down to form an ulcer.

Because phlyctenulosis is frequently associated with eczema, the term "eczematous conjunctivitis" was used to designate this conjunctival disease. Older authors, such as Scarpa and Mackenzie, used the term "scrofulous ophthalmia" to describe phlyctenular disease of the eye. Scrofulous conjunctivitis or keratitis is still a favorite term among some authors, since the disease has a tendency to involve the glands. It is the most common ocular disease among the children of Europe.

In China, Wang [54] studied its occurrence in Shanghai; of 4,292 patients treated in the clinic in 1931, 819, or 19.1 per cent, were scrofulous. The highest incidence was between April and July. Wang stated that weather and living conditions were the direct cause of the high incidence of scrofulous disease in China during these months. More men than women were affected, and the disease was more common in adults than in children. Wang found that 92 per cent of his patients responded to the Mantoux test. He stated that phlyctenulosis has a nonspecific anaphylactic basis in persons with tuberculous diathesis.

Leber [55] was first to state that phlyctenular disease of the eye is caused by tuberculous toxins reaching the eye through the blood stream, apart from the bacilli themselves. He based his opinion as to the tuberculous nature of the conjunctival disturbance on the occasional occurrence of crops of phlyctenules after the injection of tuberculin.

Evidence supporting the relation of phlyctenular disease to tuberculosis has since been produced by Weekers [56] and Loddoni.[57] They demonstrated that phlyctenulosis may be produced by instillation of tuberculin in the conjunctival sac of persons who are hypersensitive to the tubercle bacillus. It may also be produced in animals which are hypersensitive to foreign protein, horse serum, for example, by instillation of such a substance in the conjunctival sac. They admitted, however, that other substances may quite possibly be responsible for phlyctenulosis in certain persons.

Ajo,[58] of the Ophthalmic Clinic at the University of Helsingfors, Finland, observed 367 patients, of a total of 449 with phlyctenular disease, in a period of fifteen years (1912-1927). Tuberculosis was the cause of death in 35 of the 55 fatalities and was the probable cause of death of 4 other patients, the mortality rate for tuberculosis being thus 10.62 per cent. Of the 100 living patients still under his care at the end of the experiment, 50 were free from the disease. Of the remaining 50, 39 showed tuberculous changes; 5, changes which were probably tuberculous, and 6, other pathologic changes. Pulmonary tuberculosis was observed in 7 patients. Ajo expressed the opinion that patients with phlyctenular disease may have a severe form of tuberculosis later in life.

Giannantoni and Possenti [59] studied 150 patients with clinical and roentgenologic signs of pulmonary tuberculosis. The ages of the majority ranged from 20 to 50, phlyctenular conjunctivitis occurring in 22.66 per cent and follicular hypertrophy in 30 per cent of the patients. Sties, chalazion and blepharitis were

53. Benalioua: La primo-infection tuberculeuse de la conjunctive, Ann. d'ocul. **175**:746, 1938; abstracted, Arch. Ophth. **21**:877 (May) 1939.

54. Wang, C. L.: Zur Statistik und Pathologie der skrofulösen Augenentzündungen in Shanghai, Klin. Monatsbl. f. Augenh. **93**:505, 1934.

55. Leber, T.: Arch. f. Ophth. **3**:251, 1884; cited by Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, p. 2318.

56. Weekers, L.: Phlyctènes oculaires et tuberculose, Arch. d'opht. **44**:342 and 411, 1927; L'anatomie pathologique des phlyctènes oculaires, Bull. Acad. roy. de méd. de Belgique **24**:435, 1910.

57. Loddoni, G.: Cherato-congiuntivite flittenulare e allergia, Ann. di ottal. e clin. ocul. **58**:28, 1930.

58. Ajo, A.: Zur Frage des späteren Schicksals der Phlyktänulosepatienten mit besonderer Berücksichtigung der Tuberkulose, Acta ophth., 1938, supp. 15, p. 1.

59. Giannantoni, C., and Possenti, G.: Sintomi oculari nella tubercolosi polmonare, Ann. di ottal. e clin. ocul. **61**:823, 1933.

frequent among the younger patients. The authors also observed primary lesions in the chest in 80 per cent of the patients with disease of the uveal tract.

Fontana[47] observed tuberculosis in the lungs in 50 per cent of cases of phlyctenular conjunctivitis. He concluded that there is a close association between phlyctenular conjunctivitis and tuberculosis. This opinion was shared by Riehm, who stated that phlyctenular keratoconjunctivitis for the most part, particularly in Europe, has tuberculosis as the basic cause.

In England, Harman's observations on phlyctenular conjunctivitis showed that the disease was benign, and not of tuberculous origin. He stated[60]:

> The records show that disease occurs during the fourth to the seventh year, with maximum incidence in the fifth year. It is a disease of the poor and ill fed. In Belgrave Hospital for children, during a period of ten years, one half of the children were cured in one week; three fourths were well in a fortnight; and all except a small group of three per cent, who developed severe keratitis, were cured by the sixth week.

The contents of the phlyctenules were examined in 23 cases. In 21 cases they proved to be sterile. Harman concluded that the phlyctenulosis was a herpetiform eruption produced by chronic irritation of the collateral branches of the fifth nerve in debilitated children and that it had no essential relation to the tubercle.

Harman significantly remarked[60]:

> . . . no one would hesitate to acknowledge that phlyctenular conjunctivitis would be likely to appear in tuberculous disease, even as it does in those who are ill-fed and debilitated, but I think the evidence indicates that the direct exciting cause is the irritation of the fifth nerve by nasal and oral sepsis in these weakened children.

With respect to tuberculosis of the interior portion of the uvea—the iris, the ciliary body and the choroid—the inflammation of the iris can easily be seen. The inflammatory process of the ciliary body in tuberculous ocular infection is sufficiently distinct to be diagnosed, particularly when the changes are of long duration and are gross. The evidences of tuberculosis of the choroid, however, are not apparent until after removal of the eye.

Nias and Paton[61] (1906), in a study of a series of cases of phlyctenular conjunctivitis, observed that the opsonic indexes to the tubercle bacillus were practically normal; no tuberculous lesions in the body were demonstrable in these cases.

Tejeda[62] studied 100 cases of phlyctenular ophthalmia with respect to the relation of the disease to tuberculosis, the history, the clinical symptoms, the reaction to tuberculin and the roentgenographic evidence being considered. After reviewing the histories, the author concluded that the relation between phlyctenular conjunctivitis and tuberculosis was not established. He found a positive reaction to tuberculin in 86 cases. In his opinion, the great frequency of a positive tuberculin reaction in cases of phylctenular conjunctivitis is not conclusive evidence of any relation to tuberculosis.

The predominant opinion of American observers is that this disease bears little relation to tuberculosis. The fact that phlyctenular conjunctivitis has greatly decreased with the improvement of living conditions, better dietary standards and administration of vitamins adds weight to the belief that the disease is the result of faulty metabolism.

The relation of phlyctenulosis to the enlargement of the glands of the neck led many authors to the belief that ocular disease is associated with tuberculosis of the glands rather than with tuberculosis of the lung. Werdenberg,[63] in a study of 500 patients, detected mild tuberculosis of the glands in 60 per cent, roentgenographic evidence, without clinical signs of tuberculosis of the lung, in 30 per cent and clinical pulmonary disease in 10 per cent. From these observations, he concluded that the mode of infection of the eyes is not by flooding of the blood stream with a large number of bacilli but, rather, by slow passage of a small number of bacilli from a quiescent focus to the ocular tissues. Grönholm,[64] in a study of 100 patients with ocular tuberculosis, observed that 55 per cent had infected glands and 18 per cent tuberculosis of the lungs.

Because involvement of the glands has been noted in most patients with scrofulous ophthalmia, the opinion has been expressed by many observers that phlyctenular disease frequently noted in children is an early symptom of tuberculosis. Völkel,[65] of Freiburg, observed 12 allegedly tuberculous children in an institution. Seven presented evidence of exudative lymphatic diathesis. These children had hypertrophic pharyngeal and palatine tonsils, palpable cervical

60. Harman,[31] pp. 130-142.

61. Nias, J. B., and Paton, L.: Contribution to Study of Phlyctenular Conjunctivitis, Tr. Ophth. Soc. U. Kingdom **26**:232, 1906.

62. Tejeda, M.: Conjunctivitis flictenular y tuberculosis, Arch. de oftal. hispano-am. **32**:*219, 1932.*

63. Werdenberg, E.: Neuere Gesichtspunkt zur Beurteilung und Behandlung der Augentuberkulose, Schweiz. med. Wchnschr. **59**:*126, 1929.*

64. Grönholm, V.: Ocular Tuberculosis and Constitution, Acta ophth. **6**:*297, 1928.*

65. Völkel, R.: Tuberculosis of the Eye in Children, Arch. Ophth. **23**:419 (Feb.) 1940.

glands, a tendency to eczema, large hilar glands, evident roentgenographically, and impaired physical condition. Two of the children suffered from general scrofula. In the patients with chronic recurrences, the condition in the eye paralleled the changes in the general condition. Recurrences, with simultaneous involvement of the affected cervical glands and joints, were said to be due to hematogenous dissemination.

In view of the variations in the laboratory data and the clinical reports, authors have tried to reconcile the apparently strange action of the tubercle bacilli. Gómez-Márquez,[66] for example, advanced the following theory:

> . . . in cases of early infection the functional defenses of the organism are increased, and not only is the bacillus overcome, but the patient is rendered immune and nonallergic. In other cases the tuberculous child also recovers from his first attack and is rendered immune, but his tissues have been sensitized, or rendered allergic, and new inoculations are followed by more or less violent inflammatory reactions, which vary according to their site and are not characteristic of tuberculosis. In still other cases the tuberculous child acquires only a partial immunity, with or without allergy. Later, if the number of bacilli attacking the child is small, he is able to resist the attack, but if the number is large, he is unable to resist the invasion, and typical tuberculous lesions make their appearance in the organs in which the inoculations take place. Among the ocular lesions of this class is parenchymatous keratitis, which is tuberculous as often as syphilitic.
>
> In the diagnosis of atypical tuberculosis, in cases in which it is impossible to find tubercle bacilli or the primary focus of infection, and in which serodiagnosis, a seroprecipitation test, determination of the opsonic index and fixation tests all give positive results, a positive Pirquet or Mantoux reaction may simply indicate a state of allergy or relative immunity originating from the primary infection.

Rich and McCordock[67] expressed the opinion that the acute inflammatory reaction evidenced by the tuberculous animal is due to sensitization of the fixed cells to tuberculoprotein and is of an allergic nature. They expressed the resulting tuberculous lesion by the following formula

$$\text{Lesion} = \frac{\text{Virulence} \times \text{number} \times \text{degree of allergy}}{\text{Resistance}}$$

If the virulence and number of the invading organisms are great, the degree of allergy is high and the resistance of the patient is low, a spreading, necrotizing inflammatory reaction results. On the other hand, if the resistance of the patient is high, the virulence and number of bacilli are low and the degree of allergy is slight, a mild lesion will result.

Werdenberg and Samoilov[68] divided ocular tuberculosis into two types: (1) a "mild, productive or productive-fibrous" lesion, which tends to heal and occurs either in the stage of primary infection or in the third stage of high resistance, and (2) a "hypersensitive, chiefly exudative" type.

Urbanek[41] introduced the following classification of tuberculin sensitivity in cases of ocular tuberculosis: 1. A person who is free from tuberculosis, has never had the disease and shows no reaction to large intracutaneous injections of tuberculin or tebeprotin is said to be in a state of anergia. 2. If a healthy person is infected, the organism tends to produce antibodies, as shown by tuberculin sensitivity, or allergy. (*a*) If the course of the disease is favorable, the allergy becomes stronger as the antibodies increase, and very small doses of tebeprotin cause a positive reaction. (*b*) When the tubercles become encapsulated and bacilli disappear from the rest of the body, the degree of allergy diminishes and, with complete healing, is changed into a positive anergia, the result of destruction of bacteria. (*c*) In cases of severe disease the original allergy becomes progressively weaker, with an increase in toxin and a decrease in formation of antibodies, until the latter completely ceases and a negative anergia is present, the result of the complete destruction of all the defensive powers of the organism. In this state death may result from injection of the tuberculin.

Woods[69] stated that allergy and immunity influence to a high degree the type of lesion which results from infection of the tubercle bacilli. When the normal animal is inoculated with tubercle bacilli, it shows a progressive, sluggish development of generalized tuberculosis, with formation of tubercles. When the tuberculous animal is so inoculated, an acute inflammatory reaction, with caseation and necrosis, results. In persons with high resistance and a low degree of allergy, tubercle bacilli lodging in the eye apparently cause lesions which are nonspecific in their appearance and have a tendency to become circumscribed and to heal. On the other hand, if the patient has low resistance and a high degree of allergy, the tendency is toward inflammatory lesions of a

66. Gómez-Márquez, J.: Tuberculosis oculares típicas y atípicas, Arch. de oftal. hispano-am. **30**:17, 1930.

67. Rich, A. R., and McCordock, H. A.: Enquiry Concerning Role of Allergy, Immunity and Other Factors of Importance in Pathogenesis of Human Tuberculosis, Bull. Johns Hopkins Hosp. **44**:273, 1929.

68. Werdenberg, E.: Die Augentuberkulose im Licht der neuen Tuberkuloseforschung, Klin. Monatsbl. f. Augenh. **75**:546, 1925. Samoilov, A. J.: Principles of Specific Therapy in the Tuberculous Diseases of the Eye, Russk. ophth. j. **12**:145, 1930.

69. Woods, A. C., in Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, p. 1183.

spreading, necrotizing type. Also, if the number and virulence of the organism are great, lesions, such as tuberculoma of the anterior or the posterior portion of the uveal tract, will result, with a pronounced inflammatory reaction and a tendency to spread, caseate and ultimately perforate the eyeball. These are the characteristics of tuberculous lesions.

SUMMARY AND CONCLUSION

From the varied opinions cited, it is evident that the relation of ocular tuberculosis to tuberculosis of other organs, particularly the pulmonary form, has not been definitely established. The positive reaction to the Pirquet or Mantoux test can no more serve as evidence on which to ascribe chronic ocular lesions of an obscure nature to tuberculosis of some other organ of the body than can the positive Widal reaction account for all complications of typhoid. A favorable response to the tuberculin test, likewise, is no proof of the diagnosis; other foreign proteins may equally well ameliorate the ocular condition of certain patients, and all too often the conclusion is based on the fallacy of sequence of events—*post hoc, ergo propter hoc.*

Before tuberculin was brought to the attention of the medical profession, the diagnosis of tuberculosis of the eye was based on the presence of a similar condition elsewhere in the body. The diagnosis was established in much the same way as is syphilitic infection of the eyes, namely, on the basis of a clinical and laboratory report of syphilis. When tuberculin came into use, its diagnostic value became of permanent importance. The diagnosis of tuberculosis was based on a positive reaction. Later, when it was shown that the intradermal test with tuberculin was not infallible, arguments in its defense appeared in the ophthalmologic literature.

A generation ago focal infection was accepted as an etiologic factor in obscure ocular disease. Later endocrinopathy was hailed as an explanation of morbid conditions of uncertain origin. Now allergy is being stretched to the limits as an etiologic factor in many ocular complications the cause of which cannot be detected by the usual scientific methods. One theory after another has been advanced to show the diagnostic merits of tuberculin, none of which, however, have fitted into the scheme of the etiologic diagnosis of all obscure diseases of the eye. The fact remains that the eye appears to possess an immunity against active pulmonary tuberculosis, and a positive reaction to tuberculin does not indicate where the lesion is located.

Formerly, ocular lesions of doubtful origin were designated as idiopathic—a frank confession that the cause was not known. In this scientific age one must have a cause for everything, any kind of a cause, even if it is unscientifically conceived. This inability to say "I don't know" appears to be the most regrettable trait of modern medicine, and this is peculiarly true with respect to ocular tuberculosis.

From the literature cited, certain facts are evident: 1. Phlyctenular keratoconjunctivitis is not usually of tuberculous origin. 2. Tuberculous lesions of the eye are not nearly as common as they are generally supposed. 3. Uveal tuberculosis is not necessarily seconday to tuberculosis elsewhere in the body. The fact that the ocular tuberculosis frequently leaves the lungs undamaged shows that the tubercle bacillus may enter the blood stream and attack the eye directly. 4. The nature of an infection in the anterior segment should always be determined in the laboratory. When it is impossible to obtain a specimen of the uveal tissue, a provisional diagnosis may be made by microscopic study of the lesion, by the general tuberculous status of the patient and by exclusion of other etiologic factors. Tuberculin tests are of value only when associated with other features of the case.

1616 Pacific Avenue.

Obituaries

CARL HAMBURGER
1870-1944

Dr. Carl Hamburger, who died in May 1944, was born in 1870. He graduated in 1893 and spent several years in general hospital service and in the ophthalmic clinic of Hirschberg, in Berlin. It was during this period that he carried on investigations under Ehrlich.

In 1898 he settled in Berlin as oculist and gave evidence of his earnest investigations on the physiology of the eye in the publication, between 1898 and 1925, of studies on the source of the aqueous humor. He also published the results of early investigations on such subjects as the nutrition of the eyeball and tonometry. His interests were wide, and his writings, which were extensive, were not limited to ophthalmology. He was deeply interested in hygiene, not only in ocular but in communal hygiene; and in these fields, too, his contributions were numerous and valuable. His clinical studies were many and chiefly devoted to glaucoma, and his contributions concerning the therapeutic value of epinephrine for glaucoma are well known.

Dr. Hamburger was an interesting personality. His scientific interests were deep and intensive.

His wife was the daughter of the celebrated oculist Herman Cohn, of Breslau, and the sister of the well known writer Emil Ludwig.

Dr. Hamburger gave distinguished service as medical officer in the German army from 1914 to 1919. His reward was the Iron Cross—and later exile, at the age of 69. He and his wife found refuge in Geneva, Switzerland, where he continued some studies. He died at Gland, near Geneva, his wife having preceded him in death by two years.

The sorrow and tragedy of this outstanding ophthalmologist are not lessened by the fact that he is but one of many.

HARRY FRIEDENWALD.

Correspondence

VERNAL CONJUNCTIVITIS

To the Editor:—Luis Castellanos A., of Chihuahua, Mexico, published a fascinating article entitled "Ariboflavinosis as a Probable Cause of Vernal Conjunctivitis" in the March issue (ARCH. OPHTH. 31: 214, 1944). I disagree with the author's theory, which lacks scientific confirmation.

I am amazed that Dr. Castellanos has made no mention of vernal conjunctivitis as an ocular manifestation of an allergic state. The literature is replete with experimental evidence of its allergic origin. The clinical symptoms of the disease have been produced out of season by inserting in the conjunctival cul-de-sac pollens to which the patient was shown to be sensitive by intradermal tests during seasonal attacks.

The periodicity of vernal conjunctivitis in correspondence with the pollenation of the trees, grasses and weeds is no more coincidental than the onset of autumnal hay fever, which begins on or about August 15. The approach of warm weather in April coincides with the first appearance of symptoms of itching, lacrimation, redness and mucous discharge. In cases appearing for the first time in midsummer or late summer mild symptoms have been present for weeks, becoming intensified with the heat and humidity, so that the patient seeks medical relief. Prompt relief of symptoms by the use of epinephrine or epinephrine-like products is characteristic of allergic manifestations. The high incidence of positive reactions obtained by intracutaneous tests also corresponds with the incidence of such reactions obtained with other allergic manifestations. The local eosinophilia and the eosinophilia of the blood are common with vernal conjunctivitis, as they are with other forms of allergy.

It seems hardly necessary to verify a point that has already been proved beyond doubt. This becomes necessary, however, when the ARCHIVES gives conspicuous space to an article purporting to refute a recognized fact. The description of vernal conjunctivitis by Dr. Castellanos certainly differs from that which I had already published in the ARCHIVES (Lehrfeld, L.: Observations on Eighty-Seven Cases at the Wills Hosptial [1929-1931], ARCH. OPHTH. 8: 389 [Sept.] 1932; Lehrfeld, L., and Miller, J.:

Additional Research on Vernal Conjunctivitis, ibid. 21:639 [April] 1939). Dr. Castellanos does not differentiate between the limbal and the palpebral type of the disease. The former is seen largely in the Negro race in this part of the country and appears only in the spring and late summer, disappearing completely in the fall and winter. The palpebral type is described as (1) follicular conjunctivitis, (2) cobblestone conjunctivitis and (3) giant granuloma.

These three forms represent degrees in the chronicity of the disease, the first developing into the second and the second into the third, the stage depending on the duration of the disease. It is likely that the difference in Dr. Castellanos' description is explained by a difference in the disease in Mexico.

There is a wide gap between the suggestion that vernal conjunctivitis is associated with ariboflavinosis and scientific proof to substantiate the theory. Dr. Castellanos fails to offer any data on the levels of riboflavin in the urine in patients under his care. Bulletin No. 109 of the National Research Council, entitled "Inadequate Diets and Nutritional Deficiencies in the United States," published in November 1943, states that riboflavin deficiencies can be determined by urinalysis.

My Mexican fellow ophthalmologist states that he obtained immediate improvement in 92 per cent of his patients after the use of riboflavin. He asserts that 35 patients showed immediate improvement on the third or fourth day and that 62 patients showed improvement in ten to fifteen days. There was no report of an actual cure. This experience differs from the observation of many investigators that a much greater time is needed for the relief of ariboflavinosis.

With regard to the use of riboflavin, I quote from the bulletin of the National Research Council:

> . . . Several investigators have used corneal vascularity as an index of riboflavin deficiency in surveys of population groups. Its validity for this purpose has been questioned, for many consider that it is not yet confirmed that all, or nearly all, of these vascular changes are due only to riboflavin deficiency or that they are a necessary accompaniment of other undoubted signs of riboflavin deficiency. The consensus of this group at the present time seems to be that one cannot assume that all significant degrees of corneal vascularization are due to riboflavin deficiency. Sandstead, following riboflavin therapy for 60 to 110 days, found no significant change in corneal vascularity which could be ascribed to this therapy; it seems doubtful that superficial vascularization of the cornea, as observed in this study and as found in the general population, should be considered a diagnostic sign of riboflavin deficiency. . . . Youmans and Patton have observed a considerable number of subjects with mild but definite corneal vascularization not accompanied by ocular symptoms and in whom there was no correlation with dietary intake of riboflavin, other dietary factors or other evidence of deficiency disease. Reexamination of these subjects showed an improvement or disappearance of the vascularization in the winter or spring season compared with the fall, in spite of a lower intake of riboflavin in the former period.
>
> . . . It has been reported that recession of the lesions of chronic ariboflavinosis is very slow and is complete only after a very long period of time.

I wish especially to call to the attention of Dr. Castellanos and the readers of the ARCHIVES that the relief of ariboflavinosis is very slow, and is not as prompt as Dr. Castellanos has reported in patients with vernal conjunctivitis, namely, in a few days. The experience of investigators proves that a deficiency of riboflavin is most common in winter and least common in summer, whereas vernal conjunctivitis is a summer disease. Never has the onset of the disease been noted in the winter. The pathologic process of the type involving the lids may carry over until winter. Despite these facts, Dr. Castellanos speaks of a vitamin deficiency in the hot season, but does not prove his point.

I wonder whether the "improvement" which the author reported was not due to his local treatment, rather than to use of the riboflavin.

LOUIS LEHRFELD, M.D., Philadelphia.

1321 Spruce Street.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Cornea and Sclera

EPIDEMIC KERATOCONJUNCTIVITIS FROM A SUBJECTIVE VIEWPOINT. T. D. ALLEN, Am. J. Ophth. 27: 16 (Jan.) 1944.

Allen described interestingly his own case of keratoconjunctivitis. He concludes that from the subjective standpoint boric acid compresses, intravenous administration of vitamin C and encouragement were the most helpful therapeutic factors.
W. S. REESE.

Experimental Pathology

A COMPARISON OF THE OCULAR REACTIONS OF PIGMENTED AND ALBINO RABBITS TO NORMAL HORSE SERUM. T. F. SCHLAEGEL JR., Am. J. Ophth. 27: 137 (Feb.) 1944.

After stating the purpose of his report and describing the procedure and results, Schlaegel draws the following conclusions:

"1. Gross and microscopic ocular reactions were essentially equal in pigmented and albino rabbits.

"2. The allergic mechanism of intraocular followed by intravenous injection of normal horse serum is less effective in producing gross and microscopic results than the method of sensitization by intradermal injection prior to injection made into the right eye.

"3. Gross and microscopic reactions were most pronounced when the intravenous followed the intraocular injection by 14 days.

"4. The microscopic picture of the injected eyes of severe reactors bore a close resemblance to that of sympathetic ophthalmia. The uveal infiltration in the non-injected eyes was very slight but present in 40 percent of the cases."

W. S. REESE.

General

OCULAR FINDINGS IN FEEBLE-MINDED MALE CASTRATES. R. G. SCOBEE, Am. J. Ophth. 26: 1289 (Dec.) 1943.

Scobee examined 17 male castrates before and after androgen therapy. He found convergence insufficiency prevalent among the feebleminded, and castrates showed a definite tendency to development of exophoria after such therapy.

W. S. REESE.

THE GEOGRAPHICAL DISTRIBUTION OF OCULAR INFECTIONS. C. WEISS, Am. J. Ophth. 27: 175 (Feb.) 1944.

Weiss presents a table in which the most important infectious diseases of the eye are arranged according to broad geographic zones.

W. S. REESE.

Injuries

A STUDY OF MUSTARD-GAS LESIONS OF THE EYES OF RABBITS AND MEN. I. MANN and B. D. PULLINGER, Am. J. Ophth. 26: 1253 (Dec.) 1943.

Mann and Pullinger draw the following conclusions:

"1. The clinical pathology of the lesion involving the limbus is similar in man and the rabbit.

"2. The reaction in man and the rabbit is dependent on the size of the dose and the anatomic situation. The effects of vapor and liquid are different only when the actual amount of mustard gas which soaks into the tissues is different; that is, the difference is quantitative only.

"3. The late keratitis in man is seen as a degenerative ulceration depending on the initial damage sustained by the limbus and cornea, and not on any continued action of mustard gas or any of its breakdown products.

"4. From 3 it follows that in the present state of our knowledge prophylaxis is likely to be much more important than treatment. It is very difficult to assess the value of treatment in man, since the dose of mustard gas received can never be known, and no two cases will be comparable. Two eyes of the same patient may be comparable although by no means always, even when the lesions are due to vapor."

W. S. REESE.

NONPENETRATING INJURIES OF THE EYE. Z. MARKELOVA, Vestnik oftal. 22: 27, 1943.

The ratio of nonperforating to perforating injuries of the eye in hospital X was 58: 42. The lid and the cornea were most frequently injured, while the sclera and the conjunctiva were rarely involved. Erosions of the cornea were observed in about 30 per cent of cases. Deep injuries of the cornea (70 per cent) were complicated by iritis or iridocyclitis, which required hospitalization until complete recovery. Injuries with fragments were predominant (94 per cent); next

in order were blind, penetrating and gunshot injuries. If the foreign body was in the soft tissues of the lid or muscle and did not cause inflammatory symptoms, it was left alone. In the case of blind and of penetrating injuries of the soft tissues edema of the tissue was frequently not present. Plastic operations had to be done in 14 of 57 cases. Cataract and retinal detachment were the more severe complications. Cataract extraction was done in cases without inflammatory signs; otherwise the patients were evacuated to rear hospitals.

O. SITCHEVSKA.

Neurology

INCLUSION BODIES AND LATE FATE OF GANGLION CELLS IN INFANTILE AMAUROTIC FAMILY IDIOCY. O. MARBURG, Arch. Neurol. & Psychiat. 49: 708 (May) 1943.

Investigation of several cases of infantile amaurotic family idiocy has revealed the existence of inclusion bodies and severe secondary cell degeneration. The inclusion bodies are partly argentophilic and partly argentophobic, the reaction depending on the kind of fat which forms their basis. In cases in which inclusion bodies are present there are almost always myoclonic states.

Precipitations outside the cells are due to degeneration of axons. It cannot be definitely decided whether precipitations have their origin in the tissue fluid as well (Alzheimer and Sturmer).

The clinical signs in a case of infantile amaurotic family idiocy are due only in part to the well known cellular changes, which affect merely the vegetative, and not the functioning, portion (fibrils). Only when the functioning part also is affected do neurologic signs appear.

The atonic asthenia, like that of myasthenia or of Addison's disease, is to be explained by a disturbance in cholinergic and adrenergic factors, obviously the result of changes in the thymus and the adrenals which are observed with infantile amaurotic family idiocy.

R. IRVINE.

ANEURYSM OF THE CIRCLE OF WILLIS, WITH SYMPTOM-FREE INTERVAL OF TWENTY-SEVEN YEARS BETWEEN INITIAL AND FINAL RUPTURE. S. ROSEN AND W. KAUFMANN, Arch. Neurol. & Psychiat. 50: 350 (Sept.) 1943.

Today it is well accepted that the interval of freedom from symptoms following the first attack of aneurysmal rupture may be days, months or years.

The case reported here is that of a man with an interval of twenty-seven years between the first symptoms of rupture of an aneurysm of the circle of Willis, associated with unconsciousness and xanthocromia of the cerebrospinal fluid, and the final, and fatal, episode. A survey of all the reported cases of this condition (table) reveals that twenty-two years is the longest interval of freedom from symptoms on record.

R. IRVINE.

PROGNOSIS OF MULTIPLE SCLEROSIS. H. MCINTYRE and A. MCINTYRE, Arch. Neurol. & Psychiat. 50: 431 (Oct.) 1943.

"A clinical study of the prognosis of multiple sclerosis, based on the life charts of 55 patients, beginning with the initial episode, is presented. Three types of disseminated sclerosis are recognized: the acute, the remittent and the chronic progressive.

"The clinical course in a case of Devic's disease (neuromyelitis optica) did not appear to differ from that of the remittent type of multiple sclerosis.

"Twenty-seven patients had optic neuritis at some stage of their disease. In only 1 patient, however, were both optic nerves affected at the same time. The prognosis for the optic neuritis of multiple sclerosis is generally good; only 1 of the patients became completely blind. Optic neuritis may usher in the disease or, contrary to some opinions, may occur later in its course, years after other episodes have supervened. Seven patients showed visible swelling of the optic nerve.

"The prognosis is good for the individual attack in the remittent form of multiple sclerosis. The prognosis with respect to life is good in both the remittent and the chronic progressive form. The prognosis for life is hopeless in the acute form. Persons suffering from the remittent type may be able to lead useful lives for many years; in rare instances complete recovery occurs.

"Apoplectic episodes are not uncommon, having been experienced by 12 to 50 patients with the remittent type. The percentage probably would be higher if apopolectic episodes were sought for diligently in the history of all patients.

"No type of therapy advocated at present is of any value."

R. IRVINE.

MONOCULAR MYASTHENIA GRAVIS. S. S. WINTON, J. A. M. A. 122: 1180 (Aug. 21) 1943.

A girl aged 17 years complained of drooping of the left upper eyelid of sudden onset. Three weeks prior to this occurrence she had suffered from moderately severe headache and a cold in the chest. Two weeks after onset of the ptosis examination revealed no other signs of myasthenia. There were no other ocular symptoms. (No record of examination of the visual acuity, visual fields or fundus was available.) Injections of prostigmine methylsulfate, 1 : 2,000, were given

twice a week. After each injection the ptosis disappeared and the eyelid regained its normal tone and power, which effect lasted only a few hours. Later 15 mg. of prostigmine bromide was given in tablet form. After several months tolerance for prostigmine developed. The best results were obtained with a combination of 15 mg. of prostigmine bromide and 0.1 Gm. of guanidine hydrochloride, given three times daily. For the past eighteen months all symptoms have remained in abeyance. A review of the literature shows that ocular abnormalities are often only the forerunners of the full-fledged disease.

The article is illustrated.

W. Zentmayer.

Herpes Zoster Ophthalmicus—Two Rare Manifestations. T. G. Wynne Parry and G. C. Laszlo, Brit. J. Ophth. **27:** 465 (Oct.) 1943.

A woman aged 52 suddenly became blind in the right eye. Six weeks previously she had had herpes zoster along the course of the right fifth nerve. The diagnosis was acute optic neuritis. Examination of the spinal fluid showed 44 small lymphocytes per cubic millimeter and a protein content of 30 mg. per hundred cubic centimeters. Five weeks later vision was 6/60, with an absolute scotoma. The temporal portion of the optic disk showed discoloration.

A man aged 33 had had herpes on his chest six weeks previously. Three weeks later diplopia developed as a result of paresis of the right abducens nerve. The spinal fluid showed an increased cell count, with a high protein content. The paresis cleared up.

W. Zentmayer.

Ocular Muscles

The Convergence Function in Relation to the Basal Metabolism. S. V. Abraham, Am. J. Ophth. **26:** 400 (April) 1943.

Abraham attempts to show the correlation existing between the convergence function (as studied by use of the duction method) for near vision and the general health (the basal metabolism test being used as a laboratory indicator thereof).

W. Zentmayer.

The Relationship of Orthoptic Treatment to Surgery. A. DeH. Prangen, Am. J. Ophth. **26:** 1298 (Dec.) 1943.

Prangen gives the following summary:

"Restoration of function seems to be the dominant purpose in the treatment of strabismus, and the connecting link between cosmetic surgery and restoration of normal function appears to be orthoptic training.

"Accurate refraction, intensive orthoptic training, and selective surgery are the means at hand for the combating of strabismus. All are of equal importance, and maximal results should be obtained through the combined use of all in proper sequence."

W. S. Reese.

Torsion in Persons with No Known Eye Defect. T. G. Hermans, Am. J. Ophth. **27:** 153 (Feb.) 1944.

Hermans concludes that torsion is a normal phenomenon of vision and that its direction is usually a disclination at the top of the vertical meridians of the eyes relative to the median plane.

W. S. Reese.

Orbit, Eyeball and Accessory Sinuses

Emphysema of the Orbit: A Study of Seven Cases. W. O. Linhart, J. A. M. A. **123:** 89 (Sept. 11) 1943.

Seven cases of emphysema of the orbit, all occurring in soldiers with a history of recent injury, are reported. In 4 cases the condition was secondary to a blow over the eye while the patient was boxing. In 3 cases the patients were struck with a shoe, a flashlight and a mushball respectively. In 5 of the cases stereoscopic roentgenograms were taken. In none could a definite fracture line be demonstrated to communicate with the nasal cavity. There were no complications in any case.

W. Zentmayer.

Refraction and Accommodation

Effects of Astigmatism on the Visibility of Print. M. Luckiesh and F. K. Moss, Am. J. Ophth. **26:** 155 (Feb.) 1943.

Luckiesh and Moss observed that a — 0.50 D. cylinder reduced the visibility of 12 point type from 100 to 87 per cent, and a — 1.00 D. cylinder to 75 per cent, the latter representing the equivalent of loss of vision of about 4 points in type size.

W. S. Reese.

Retina and Optic Nerve

Massive Bilateral Preretinal Type of Hemorrhage Associated with Subarachnoidal Hemorrhage of Brain. L. C. Drews and J. Minckler, Am. J. Ophth. **27:** 1 (Jan.) 1944.

Drews and Minckler draw the following conclusions:

"1. A case of very extensive bilateral preretinal hemorrhage, associated with subarachnoidal hemorrhage from a congenital aneurysm of the communicating branch of the anterior cerebral.

artery, is reported. When examined pathologically, 24 days after the onset of the brain hemorrhage, only the remains of hematoma were found in the subarachnoidal space of the optic nerves. It is concluded that hematoma had been present but was absorbed.

"2. It is suggested that if a 'preretinal' hemorrhage absorbs very rapidly the hemorrhage probably is situated beneath the internal limiting membrane where the circulation may be excellent. Such a hemorrhage really should be considered intraretinal, since the internal limiting membrane is considered a part of the retina.

"3. After one or more subarachnoidal hemorrhages, adhesions may form in the cisterna basalis on one or both sides; a later hemorrhage may then fail to produce ophthalmoscopic signs in one or both eyes.

"4. As far as I can find this case presents the largest preretinal type of hemorrhage described in the literature (about 10 disc diameters, each eye). There was no evidence that blood had been forced from the supposed hematoma of the nerve sheath through the lamina cribrosa.

"5. Why do massive preretinal hemorrhages occur in subarachnoidal hematoma of the optic-nerve sheath frequently, and rarely in ordinary papilledema?"

W. S. Reese.

Vision

Visual Acuity at Low Brightness-Levels. M. Luckiesh and A. H. Taylor, Am. J. Ophth. *27*: 53 (Jan.) 1944.

The authors point out that red light is more effective for a given brightness than other illuminants and that red light has many uses in wartime, in situations where concealment is vital and dark adaptation must be maintained.

W. S. Reese.

ADDITION TO DR. HAGUE'S ARTICLE

The following note from Dr. Eliott Baldwin Hague was received too late to be added to his article which appears in this issue, page 520.

"I hope that some justification for an article considerably speculative will be found in the evidence presented that it will be worth while to inject spinal fluid from patients with active cases of this syndrome into the basal cisterna of experimental animals. I shall be pleased to cooperate with those who have cases of this syndrome under their observation."

Society Transactions

Edited by Dr. W. L. Benedict

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Alfred Cowan, M.D., *Chairman*

Warren S. Reese, M.D., *Secretary*

Oct. 21, 1943

Memoir of Dr. Griscom. Dr. Charles R. Heed.

Drusen of the Optic Nerve Simulating Cerebral Tumor. Dr. N. S. Schlezinger (by invitation), Dr. J. Waldman and Dr. B. J. Alpers.

This paper is published in full in this issue of the Archives, page 509.

Massive Skin Graft: Moving Picture Demonstration. Dr. E. B. Spaeth.

The film illustrates some of the important factors connected with a free skin graft. The patient, with a tremendous keloid involving the entire right eye, was in an extreme state of ectropion as a result of the keloid and contraction.

A subsequent attempt to make a corneal graft proved unsuccessful because of the tremendous thickening of the cornea, accompanied by severe iridocyclitis. The skin graft was simply a matter of improving the child's cosmetic appearance.

Junius Kuhnt Macular Degeneration. Dr. Samuel Altman, Philadelphia.

This paper will be published in another journal.

DISCUSSION

Dr. Charles E. G. Shannon: Dr. Knox permitted me to examine this patient several weeks ago. Two features impressed me, which were pointed out by Dr. Zentmayer in the recent discussion of the case: first, the occurrence of the macular degeneration (the juvenile type) in a man of 34, and, second, the presence of the early, or hemorrhagic, stage in the right eye and the full development of the process in the left eye.

Dr. William Zentmayer: It is rare to be able to observe both the initial and the final stage of this condition in the same patient; so Dr. Altman's case is an instructive one.

As to the origin of the fibrous tissue, it was long held that it arose from organization of the hemorrhages. Later, Verhoeff found that the pigment epithelium of the retina was also a factor in the production of the new-formed tissue.

Dr. E. B. Spaeth: The patient was referred to Wills Hospital by Dr. Andrew Knox. The photographs of the fundus were taken at Temple University by Dr. Glen Gibson. The diagnosis of the case was confirmed, on my request, by Dr. William Zentmayer.

Dr. Samuel Altman: It seems that in this disease once the damage is done and vision reaches a certain level, the condition remains stationary.

Book Reviews

Industrial Ophthalmology. By Hedwig S. Kuhn, M.D. Price, $6.50. Pp. 294, with 114 text illustrations, including 2 color plates. St. Louis: C. V. Mosby Company, 1944.

The reproach of materialism, so often brought against this so-called machine age, might be countered by citing some of its aims and achievements, idealistically inspired perhaps, yet definitely beneficial and useful. One of these is the progressive interest and activity in measures for community welfare in all its aspects, especially health, and in the active part to be taken by medicine.

While more than a little of this helpful tendency was manifest well before the flowering—if not the infancy—of industrialism, it has become at once wider and more intensive, *pari passu*, with mass production, mechanical inventions and their implications for living conditions. This has been reflected and, one might add, definitely aided by medical teaching and planning, to meet a growing demand for knowledge of the problems of social and industrial health and disease, as well as the practical details for their solution.

American ophthalmology has become aware of this situation and of the need of its cooperation in theory and practice. Although many monographs apposite to the special field of industrial ophthalmology have been published, as the author notes, here is the first comprehensive treatise on the subject.

It is authoritative, well planned and logically arranged, sound and instructive in principles and practical application and amply, as well as usefully, illustrated. Successive chapters deal with visual testing in industry (job analysis, types of teaching, tests and technic); with correction of visual defects for the job (refraction for occupation, orthoptic training, rehabilitation, economic aspects); with visual skills (types and value to management in accuracy, production and safety); visual standards and records; industrial injuries to the eyes (classification, first aid, complications); protection to the eyes; medicolegal considerations; recent advances in mechanical processes; working conditions; illumination; physical hazards to health; and the blind in industry. An appendix includes a glossary of toxic substances and their action, an ophthalmic program for industry, and a standard (approved by the American Medical Association) for the appraisal of loss of visual efficiency.

In a foreword, Dr. Albert C. Snell analyzes the visual problems confronting the industrial ophthalmologist, which include not only color vision, depth perception and special requirements of refraction, but much in the field of engineering and illumination. The same authority has contributed a chapter on "Industrial Injuries Caused by Solid Bodies," their number and cost, classification and description, as well as first aid and surgical treatment, which adds greatly to the value of this work.

The mere enumeration of these topics is evidence of the multiplicity of the problems facing social-industrial ophthalmologists, and the need for just such a work as Dr. Kuhn, an experienced worker in this field, has supplied in this well documented volume. It will be an invaluable reference handbook to all concerned with such problems.

PERCY FRIDENBERG.

Your Eyes. By Major Sidney A. Fox, Medical Corps, Army of the United States; instructor in Ophthalmology, New York University College of Medicine. Price, $2.75. Pp. 199, with 7 illustrations. New York: Alfred A. Knopf, Inc., 1944.

Preventive medicine, realizing the importance of early diagnosis for effective treatment, has been stressing a campaign of warning and information for the laity on premonitory symptoms and the essential need of professional examinations and advice. This is especially valuable in the field of ophthalmology, where apparently insignificant symptoms are ignored and ill advised self treatment, so called, is attempted only after vision has become definitely impaired. This serious situation has been dealt with by well qualified organizations, such as the National Association for the Prevention of Blindness, as well as by free lance ophthalmologists. One of these is the author of the little book under consideration, an ophthalmologist of standing and experience, who has, besides, the gift, so valuable to the popularizer in any field, of wit, a clear and illuminating style and deep interest in the needs and human nature of the lay reader.

Introductory chapters discuss in simple language how one sees, why one does not see well, sight in old age, the color world, eye glasses and the eye in traffic. Dr. Fox then turns to hygiene and first aid, ophthalmologists and optometrists and, finally, to a detailed critique of quacks and charlatans and associated rackets.

While one may question whether "the more a patient knows about himself and his ills the easier the work of the doctor becomes in preventing and curing disease," these chapters are timely and their warnings helpful.

PERCY FRIDENBERG.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6ᵉ, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6ᵉ, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, China.

Chinese Ophthalmology Society

Presdient: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

Ophthalmological Society of the United Kingdom

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Place: Oxford, England. Time: July 8-9, 1943.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

Royal Society of Medicine, Section of Ophthalmology

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

São Paulo Society of Ophthalmology

President: Dr. W. Belfort Mattos, Caixa Postal, 4086, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santa Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

Sociedad Argentina de Oftalmologia

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

Socidad Oftalmologia del Litoral, Rosario (Argentina)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive. All correspondence should be addressed to the President.

Sociedade de Ophthalmologia e Oto-Rhino-Laryngologia da Bahia

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

Società Oftalmologica Italiana

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

Société Française d'Ophtalmologie

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7^{e}.

Society of Swedish Ophthalmologists

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 III tr., Stockholm, Sö.

Tel Aviv Ophthalmological Society

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

American Medical Association, Scientific Assembly, Section on Ophthalmology

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
Place: Chicago. Time: June 12-16, 1944.

American Academy of Ophthalmology and Otolaryngology, Section on Ophthalmology

President: Dr. Lawrence T. Post, Metropolitan Bldg., St. Louis.
President-Elect: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
Executive Secretary-Treasurer: Dr. William L. Benedict, 101–1st Ave. Bldg., Rochester, Minn.

American Ophthalmological Society

President: Dr. S. Judd Beach, 704 Congress St., Portland, Maine.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.

Association for Research in Ophthalmology, Inc

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.

Canadian Medical Association, Section on Ophthalmology

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

Canadian Ophthalmological Society

President: Dr. R. Evatt Mathers, 34½ Morris St., Halifax, N. S.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.
Place: Halifax, N. S. Time: Aug. 4-5, 1944.

National Society for the Prevention of Blindness

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

Academy of Medicine of Northern New Jersey, Section on Eye, Ear, Nose and Throat

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

Central Wisconsin Society of Ophthalmology and Otolaryngology

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

New England Ophthalmological Society

President: Dr. Paul A. Chandler, 5 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. L. L. Bull, 1215–14th Ave., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. H. Pike, Midland, Mich.
Secretary-Treasurer: Dr. R. H. Criswell, 407 Phoenix Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Ray Parker, 218 Franklin St., Johnston, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. C. A. Ringle, 912–9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 526 Walton St., Macon.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St, Des Moines.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Val H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings, Mont.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr B. E. Failing, 31 Lincoln Park, Newark.
Secretary: Dr. George Meyer, 410 Haddon Ave., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.
Secretary: Dr. Maxwell D. Ryan, 660 Madison Ave., New York 21.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. L. Diven, City National Bank Bldg., Bismarck.
Secretary-Treasurer: Dr. A. E. Spear, 20 W. Villard, Dickenson.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. R. B. Maw, 699 E. South Temple, Salt Lake City.
Secretary-Treasurer: Dr. Charles Ruggeri Jr., 1120 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. William B. Agan, 1 Nevins St., Brooklyn.

Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn.

Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. Walter F. King, 519 Delaware Ave., Buffalo.

Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.

Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.

Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.

Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.

Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago.

Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.

Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.

Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. Shandor Monson, 1621 Euclid Ave., Cleveland.

Secretary: Dr. Carl Ellenberger, 14805 Detroit Ave., Cleveland.

Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.

Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.

Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. H. D. Emswiler, 370 E. Town St., Columbus, Ohio.

Secretary-Treasurer: Dr. D. G. Sanor, 206 E. State St., Columbus, Ohio.

Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. Arthur Padillo, 414 Medical Professional Bldg., Corpus Christi, Texas.

Secretary: Dr. Edgar G. Mathis, 815 Medical Arts Bldg., Corpus Christi, Texas.

Time: Second Friday of each month from October tc May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Ruby K. Daniel, Medical Arts Bldg. Dallas 1, Texas.

Secretary: Dr. Tom Barr, Medical Arts Bldg., Dallas 1 Texas.

Place: Dallas Athletic Club. Time: 6:30 p. m., firs Tuesday of each month from October to June. Th November, January and March meetings are devotec to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., De Moines, Iowa.

Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locus St., Des Moines, Iowa.

Time: 7:45 p. m., third Monday of every month fron September to May.

Detroit Ophthalmological Club

Chairman: Dr. Raymond S. Goux, 545 David Whitne Bldg., Detroit 26.

Secretary: Dr. Arthur Hale, 1609 Eaton Tower, Detroi

Place: Club rooms of Wayne County Medical Society Time: 6:30 p. m., third Thursday of each mont November through April.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave Detroit.

Secretary: Dr. Leland F. Carter, 1553 Woodward Ave Detroit.

Place: Club rooms of Wayne County Medical Societ Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.

Secretary-Treasurer: Dr. Joseph L. Holohan, 330 Stat St., Albany.

Time: Third Wednesday in October, November, Marcl April, May and June.

Eastern Pennsylvania Association of Eye, Ear, Nose and Throat Physicians

President: Dr. James E. Landis, 232 N. 6th St Reading.

Secretary-Treasurer pro tem: Dr. Paul C. Craig, 23 N. 5th St., Reading.

Time: Last week in April each year.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. Rex Howard, 602 W. 10th St., For Worth, Texas.

Secretary-Treasurer: Dr. R. H. Gough, Medical Art Bldg., Fort Worth, Texas.

Place: Medical Hall, Medical Arts Bldg. Time: 7:3 p. m., first Friday of each month except July an August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.

Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.

Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.

Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.

Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.

Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.

Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.

Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.

Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. M. E. Trainor, 523 W. 6th St., Los Angeles.

Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time. 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.

Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Edwin C. Bach, 324 E. Wisconsin Ave., Milwaukee.

Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.

Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.

Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.

Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.

Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.

Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.

Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashvile, Tenn.

Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.

Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Oto-laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.

Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.

Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Frank C. Keil, 660 Madison Ave., New York.

Secretary: Dr. Willis S. Knighton, 121 E. 61st St., New York.

Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. Milton Berliner, 57 W. 57th St., New York.

Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.

Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.

Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.

Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. D. D. Stonecypher, Nebraska City, Neb.

Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.

Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.

Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.

Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.

Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.

Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. John B. McMurray, 6 S. Main St., Washington, Pa.

Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.

Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

READING EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. R. M. Brickbauer, Shillington, Pa.

Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.

Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.

Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.

Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.

Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. C. C. Beisbarth, 3720 Washington Blvd., St. Louis.

Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd., St. Louis.

Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.

Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.

Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.

Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.

Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.

Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.

Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.

Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.

Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.

Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.

Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. E. W. Campbell, 316 Michigan St., Toledo, Ohio.

Secretary: Dr. L. C. Ravin, 316 Michigan St., Toledo, Ohio.

Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.

Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.

Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. S. Bockoven, 1752 Massachusetts Ave., Washington, D. C.

Secretary-Treasurer: Dr. John Lloyd, 1218–16th St. N. W., Washington, D. C.

Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.

Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.

Place: Office of chairman. Time: Last Tuesday of each month from October to May.

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